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SPACE BIOLOGY AND AEROSPACE MEDICINE

VOL 20, NO 2, MARCH-APRIL 1986

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PHILOSOPHICAL ASPECTS OF ADAPTATION THEORY

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[Article by B. S. Alyakrinskiy]

[English abstract from source] This paper discusses the general concepts of the problem of adaptation from the dialectic point of view which, according to F. Engels, is the most important pattern of thinking in natural sciences. Dialectics provides an analog and therefore a method for interpreting developmental processes, universal relationships in nature, transition from one area of research to another. From the point of view of dialectic laws adaptation acts as a contradictory process of habituation to various environments. The contradictory pattern of the adaptive process and its result is very distinct in terms of heredity and variability. A logical enlargement of the concept of adaptation is the transition to the study of homeostasis which is assumed to be its mechanism, a property which has developed in the course of evolution and fixed in heredity. This adaptive property is contradictory in its essence because homeostasis is a unity of stability and instability, a fluctuating constancy. In addition to the law of constancy of the inner milieu, there is a law of homeostatic deviations. This concept can be understood through an analysis of the system theory that includes a continuous variation and conservation of structure which indicates its ordered oscillation, that is, its rhythmicity. This clarifies the relationship between homeostasis and biological rhythmicity as a method of maintaining the former. Thus, a consistent analysis of the problem of adaptation can help identify transition from one area of research to another, specifically to the study of oscillatory processes in living systems, including such oscillatory processes that have characteristics of universality and necessity. Such processes are biological rhythms with a period of about 24 hours, that is, circadian rhythms.

[Text] It is rather important to natural science (particularly contemporary) to have a philosophical interpretation of one of the rather complicated

problems of biology and medicine, the problem of adaptation. There is no need to go back to the period of inception of this problem. Such an excursion would lead us to the works of Aristotle and, through a long series of investigations and interpretations of the adaptation phenomenon, to current conceptions of its essence. True, even at the present level of our knowledge there is still no common point of view and, consequently, no single definition of adaptation, although the general opinion that adaptation is adjustment to the environment that surrounds an organism (population) is shared by virtually all researchers. This is, for example, the definition of physiological adaptation offered in the "Great Soviet Encyclopedia" ["Bolshaya sovetskaya entsiklopediya"]: "Physiological adaptation is the aggregate of physiological reactions that is the basis of the body's adjustment to change in ambient conditions, and it is aimed at preserving relative stability of its endogenous environment--homeostasis" [2].

This definition is one of the few in which adaptation is linked with homeostasis. At the same time, it is close to definitions in which self-containing significance is attributed to the factor of "being adjusted" to the environment, a balance with it. Such interpretation of the adaptation phenomenon creates the impression of harmonious unity of the body and environment, and the concept of harmony is extrapolated to the body itself; the opinion is formed that an organism harmoniously combined with the environment is notable for the same harmony as well in the combination of its functions and processes that constitute its vital basis.

However, such a view of the organic world harmoniously balanced with the environment and just as harmonious in its endogenous environment is a lifeless copy of nature, the result of a unilateral, nondialectical approach to the problem of adaptation of an organism to the environment, which is typical of ordinary, formally logical, rational thinking. With such facts in mind, Hegel wrote: "As a conception, present existence (in our case, present existence should be construed as the achieved degree of adaptation, its result."--B.A.) is first viewed as something simple and positive, and at the same time as something that calmly resides within its boundaries. True, we also know that everything finite (as is present existence) is subject to change. This variability of present existence is, however, viewed as only a possibility, the realization of which has no grounds in it. In fact, however, variability is contained in the concept of present existence, and change is merely the discovery of what present existence is" [5].

Harmony between an organism and the environment is only a conception, beyond which there is a contradiction that is not always clearly detectable. And it is opportune to cite here another definition of adaptation, according to which "... adaptation is the expression of unity of the endogenous (organism) and exogenous (environment) with its inherent contradictory elements" [7]. Analysis of these contradictory factors inherent in adaptation makes it possible to determine its essence.

We should recall the dialectical contradiction of the very concept of adaptation, since adaptation is in essence both a process and a result, i.e., the unity of the two; hence, adaptation cannot emerge as an episodic phenomenon, and one related to extreme situations at that. In fact, the concepts of

"vitality" and "adaptation" are the same, they coincide, and this is why adaptation is a continuous process.

Continuity of the adaptation process had been repeatedly stressed when discussed from the standpoint of phylogeny, evolution, when the concept of adaptation was based on the historical (evolutionary) principle, which takes into consideration the genesis proper of this phenomenon [7], since, as I. I. Shmalgauzen wrote, "the effect of the same homeostatic mechanisms is manifested by historical transformations, and evolution itself turns out to be a controllable process of continuous adaptation" (quoted by A. B. Georgiyevskiy et al. [7]). Incidentally, we should like to mention that there is validation to the statement that hereditary variability was the result of evolution and was refined in the course of evolution as adaptation [7].

To return to the problem of unity of process and result in the adaptation phenomenon, it should be stressed that this unity had been noted by many authors who used different terminology. For example, I. I. Shmalgauzen introduced the concepts of stabilizing and moving forms of selection, the former preserving the established norm, polishing the "adaptive norm" (expression of I. I. Shmalgauzen) by means of small mutations, causing its more reliable reproduction and eliminating deviations. N. P. Dubinin wrote: "Shmalgauzen is quite right in singling out ... the stabilizing form of selection, i.e., strengthening, stabilization of development of already present historically developed useful properties of organisms. Apparently, genotypic evolution proceeds through selection of mutations that refine the type of development" (quoted by A. B. Georgiyevskiy et al. [7]). The moving form of selection alters, disrupts the "adaptive norm" and forms a new one.

The unit of process and result is expressed in the unity of heredity and variability, about which F. Engels wrote: "... starting with a simple cell, each step forward to the most complex plant, on the one hand, and to man, on the other, is taken through the constant struggle between heredity and adaptation" [38], and "one can view heredity as the positive, conserving side and adaptation, as the negative one that constantly destroys inherited characters; but we would be equally justified in viewing adaptation as creative, active, positive activity and heredity, as passive, negative activity that offers resistance" [38].

In actuality, there is realization of the complex dialectics of relations between living systems and the environment, the contradiction between which is the foundation of the process of life, through the unity of process and result, stabilizing and moving forms of selection.

If we were to approach the problem of unity of organism and environment from the standpoint of contradiction of this unity, we could say that the environment contains all that is necessary to life of an organism and all that is necessary for its death. In other words, the genetic program is deployed in constant interaction with various deleterious factors, and the large number of such factors is an important prerequisite for development of the individual [7].

Turning to the language of philosophy, it can be said that unity of the organism and environment is based on unity of attraction and repulsion. F. Engels writes: "... the basic form of any movement is approximation and separation, compression and expansion, in brief, the old polar opposition of attraction and repulsion" [38]. With reference to the relationship between attraction and repulsion, he stresses that expressly "... repulsion is actually the active aspect of motion and attraction, the passive" [38]. "Hegel," observes F. Engels, "is ingenious even in that he derives attraction as the secondary element from repulsion as the primary one...." [38]. It is interesting to note that C. Bernard, basing himself on physiological data, wrote: "Disorganization and disassimilation deplete living matter in organs that are in a functional state; assimilation synthesis regenerates tissues.... These two operations of destruction and renewal are opposites of one another, but they are also definitely inseparable in at least the sense that destruction is a necessary condition for renewal. Phenomena of functional destruction are in essence the precursors and perpetrators of material renewal...." [quoted by D. S. Sarkisov [26]).

It is hardly necessary to report the theses of H. Selye concerning the benefits of moderate stress, as well as the data of P. Patkai, M. Frankenhauser, Ye. A. Gromova et al., V. Kuznetsov, V. Zhernavkov and other researchers concerning the benefit of some imbalance between the organism and the environment [9, 15, 23, 34]. There are numerous facts of this nature. To assimilate the environment also means to disassimilate it, since adaptation in itself has the germ of deadaptation. For adaptation to a new state of the environment means elimination of what no longer corresponds to reality and preservation of the positive things achieved at the preceding stage of adaptation to the former state of the environment. Hegel wrote: "Definition of organic life consists only of the fact that, in the course of its destruction, it restores itself again and again" [6]. This restoration proceeds through negation in its dialectical meaning. K. Marx stressed: "Development cannot occur in any area without negation of its previous forms of existence" [19], referring expressly to dialectical negation. Characterizing this, V. I. Lenin wrote: "This is not bare negation, not idle negation, not sceptical negation, vascillation, doubt is typical of and relevant to dialectics, which no doubt contains an element of negation, and as its most important element at that--no, it is negation as a factor of connection, as a factor of development with retention of what is positive...." [16]. Elsewhere, commenting on the thesis of Hegel, according to which the "negative is to equal extent positive," V. I. Lenin observes: "negation is something that has a definite content, and internal contradictions lead to replacement of old content with new, higher content" [16].

The process of adaptogenesis is a convincing example of dialectical negation, since to adapt signifies to change with benefit to the living system, i.e., implementation of the development process in the broad sense of the word by means of continuous generation and resolution of internal contradictions--destruction and creation, organization and disorganization, harmony and disharmony, adaptation and disadaptation. Being the result of evolution all forms of organization contain an element of stability and, at the same time, they are subject to changes that inevitably undergo a disorganization stage--disruption of established relations. Organization and disorganization are

dialectically interrelated aspects of the same process--adaptogenesis [7]. A. A. Loginov [18] observes on this score that the principle of conflict, intrasystem and extrasystem imbalance is the basis of control and regulation of all biological systems. Control and regulation are based on internal morphofunctional asymmetry of biosystems, as well as their asymmetry in relation to the environment. The purpose of control and regulation of a biosystem is to achieve the optimum level of asymmetry necessary to maintain homeostasis of the biosystem. "We observe dialectical unity in processes of both pathogenesis and sanogenesis. Any pathology contains elements that the organism can utilize for recovery and, conversely, any protective-adaptive reaction harbors the embryo of weakening of body functions.... The possibility of converting pathology to one's benefit, the possibility of taking advantage of disturbances for protection--this ... is the organism's capacity, which developed in the course of evolution, to adapt to environmental conditions" [21]. "... It is important to the highest levels of organization," stresses V. I. Kremyanskiy, "to retain some forms of disorder; a 'well-organized' whole must always be, to some extent and in some aspects, 'a slightly' disorganized whole " [14].

Here, we cannot help but recall the thesis of Hegel: "Contradiction is what really moves the world...." [5] and the well-known formula of V. I. Lenin: "The sameness of opposites ... signifies recognition (discovery) of contradictory, mutually exclusive, opposite tendencies in all phenomena and processes of nature (including spirit and society)" [16].

To conclude this general description of adaptation from the standpoint of materialistic dialectics, we should recall the phenomenon of movement as a process of development, the reality of which is disclosed if one adheres to one of the important rules of scientific cognition--consideration of the substance through the prism of extreme opposites. G. Bruno maintained that "to get to know ... the unit of form and matter in everything--herein is the aim of reason, but to delve into this unity, to investigate all of the secrets of nature, we must investigate opposite and antagonistic ends of things, we must investigate the largest and the smallest.... There are countless forms and types of development between these poles...." [quoted by V. K. Bakshutov [1]). In our case, such extreme opposites of maximum and minimum are maximum harmony of the organism and environment, maximum possible merging with it, absolute adaptation of the organism, on the one hand, and utter incompatibility with the environment, utter disharmony with it, on the other [1]. Adaptation is always development, motion. To develop means to always accumulate something and, accordingly, lose something. This is why we often speak, for example, of the development of good and bad tendencies in man. In the latter case, he accumulates what is bad and loses what is good, but this is also movement between two poles in the direction away from the "absolute good" to the the "absolute bad." All movement between two extreme states inevitably includes both, to some extent or other, which allows us to refer to the unity of opposites, their identity, but identity in the sense not only of result, but process in which the law of negation of negation is reflected, as particularly stressed by V. I. Lenin, starting with a description of the ideas of development with expressly this law [17].

In analyzing dialectics of adaptation, we should return to its link with the phenomenon of homeostasis. First of all, we must recall the cited thesis of I. I. Shmalgauzen to the effect that there is manifestation in historic transformations of the effect of homeostatic mechanisms, and that evolution itself is a process of continuous adaptation. In their book, "Strategy of Biochemical Adaptation," P. Hochachka and G. Somero discuss the phenomenon of vector homeostasis, the essence of which consists of the fact that, "in the course of adaptation to the environment, both rate and direction of metabolic processes are so 'attuned' that the body continuously receives the products it requires" [35]. G. L. Shkorbatov (quoted by A. B. Georgiyevskiy [7]) offers opinions of adaptation as an aggregate of reactions directed toward maintaining the functional constants of living systems when they are exposed to changing environmental conditions, i.e., views of adaptation as a phenomenon of homeostasis (dynamic equilibrium under prevailing environmental conditions) that is widespread in nature.

"In offering the characteristics of the historic basis of the teaching on homeostasis, it must be stated that the phenomenon of homeostasis is, in essence, an evolutionarily developed, genetically fixed adaptation property of an organism to ordinary environmental conditions ... reactions that provide for homeostasis may be directed toward maintaining certain levels of a stationary state, coordination of complex processes to eliminate or limit the effects of deleterious factors, toward development or preservation of optimum forms of interaction between an organism and the environment under altered living conditions. All these processes determine adaptation" [8]. We should emphasize in particular that any form of adaptation is developed on the basis of homeostatic mechanisms. "... The concept of homeostasis refers not only to a certain constancy of different physiological constants of a living system. It includes processes of adaptation and coordination of physiological processes that provide for the unity [integrity] of the organism under both normal and altered living conditions" [8].

In essence the concept of homeostasis is profoundly dialectical, since it implies unity of states of stability, constancy and mobility, variability, which is why a new concept of homeokinesis arose. But the essence of homeokinesis is manifested more by limitation of its inherent variabiltiy, this fluctuation, than by this variability. It is opportune to recall here the thesis of W. R. Ashby [39] to the effect that all organization is also some restriction and that organization is good if it renders the system stable with regard to a certain state of equilibrium. However, this thesis should not be interpreted literally. Ashby's thesis has a direct bearing on the result of adaptation. If, however, we take into consideration the essence of the adaptation process itself from the standpoint of its homeostatic distinctions, the element of impaired restrictions also acquires importance, as stressed specially by Yu. Uryvayev in "Harmony of Living Regulation." He writes: "... it is important to an organism not only to stabilize endogenous constants but also, to some extent and for a certain time, to put them out of balance, thereby conditioning all homeostatic systems" [33]. The fact that the boundaries of homeostasis change under certain special conditions is a good example in this respect. Thus, G. N. Kassil reports that, in athletes (particularly those with high qualifications), the boundaries of homeostasis at rest, during training and competitions are set within a different and considerably wider range than in individuals who

are not involved in sports. This author writes: "Homeostasis is, in essence, a special instance of the law of preservation of matter and energy. In the broad dialectical sense, it covers successive phases and cycles of vital functions, each of which has its own distinctions" [13].

Some interesting data about the dynamics of homeostasis were obtained in studies of the process of human adaptation to high latitudes [22]. It was found that, in the course of such adaptation, there are changes in protein and lipid spectra of blood, while levels of some hormones, vitamins, macro- and trace elements, even blood sugar, often drop beyond the bottom range of the conventional norm. The body changes to a new level of homeostasis. A different endogenous environment is formed, with different physicochemical characteristics.

With reference to this interpretation of homeostasis, it is opportune to recall the theses that are being developed by V. M. Dilman concerning the dynamics of homeostasis during development of a living system. Analyzing, in particular, the dynamics of sensitivity of the hypothalamus, he shows that, after birth, the hypothalamus has maximum sensitivity to the inhibitory effect of sex hormones, and for this reason the sex center of the hypothalamus is inhibited in this period by the small amount of sex hormones that are already being produced by the immature organism. Then comes a period of activity of reproductive function, when the threshold of sensitivity of the hypothalamus to the inhibitory effect of sex hormones rises, which leads to stimulation of reproductive glands and increase in concentration of sex hormones in blood. However, this does not lead to their inhibition of the sex center of the hypothalamus, since the threshold of its sensitivity continues to rise, and it is relieved again and again of the inhibitory effect of these hormones. This is how the strength of the reproductive system increases and, at the same time, there is retention of the mechanism of self-regulation inherent to the homeostatic system.

Consequently, along with a mechanism aimed at maintaining equilibrium and constancy (homeostasis), there is a mechanism of disrupting them, which implements the program of development of an organism. "And, while stability of the body's endogenous environment is the law of its existence, programmed disruption of homeostasis is the law of its development. The law of constancy of the endogenous environment coexists with the law of deviation of homeostasis" [10]. Long-term preservation of reproductive function, which corresponds to the action of the law of constancy of the endogenous environment, is provided by compensatory increase in synthesis of sex hormones (which is stimulated by the hypothalamus as it progressively raises the threshold of its sensitivity to inhibition by these hormones), i.e., this is achieved by fulfillment of the opposite law, the law of deviation of homeostasis. The author remarks: "This is really the unity of opposites, of opposites that are so well-concealed that there external manifestation appears more than beneficial" [10].

In analyzing the hormonal mechanisms of adaptation and conditioning, A. A. Viru stresses: "In a number of instances we find that, to provide for constancy of one parameter, it is necessary to temporarily, but always rather significantly remove other parameters from an always stable level. Sometimes, the body "sacrifices" the constancy of its endogenous environment

for the sake of providing conditions necessary to life. In all these cases, the organism must be removed from the limits of resting homeostasis to new levels of homeostasis" [4]. There is no need to delve into the details and fine points of the problem of homeostasis. This is a job for the special sciences, since, as observed by D. S. Sarkisov, "whatever the special problem of concern to a researcher, ... he cannot fail to touch upon, to some extent or other, on problems of adaptation, adjustment, interaction of different biological processes, compensation of impaired functions, etc., which constitute special issues ... of preservation of constancy of the body's endogenous environment....; at the present time, the term, 'homeostasis,' has acquired the significance of some generalizing concept reflecting all the diversity of special manifestations of relative stability of biological systems" [26].

It is valid to raise the question of content of the concept of system in the aspect, with which we are concerned. According to the most commonly used content of the concept, a system (from the Ancient Greek "whole, consisting of parts, connection") is a set of elements that are interrelated and form a certain whole, an entity [29]. When dealing with living systems, such a definition is obviously inadequate since any living system is always (expressly because it is living) active, since activity is a mandatory prerequisite for vital functions, and any form of vital activity is related to expenditure of matter and energy, i.e., dynamics and changes. And, at the same time, a living system remains, so long as it exists, expressly such a system, it is preserved by changing or changes, as it is preserved. A. M. Molchanov expresses this idea graphically: "Let us consider," he writes, "a system of equations that has a solitary state of equilibrium, and it is also stable. It appears that this is an example of a good model of a well-balanced individual. However, if we think about it more deeply, we shall find that such a system does not conform to our intuitive conception of an individual. After all, an individual does something, something happens to him, he alters his state. If, however, he arrives at a single state, this is intuitively perceived as death of the system. The system arrives to a state of stable equilibrium and ceases to be a system capable of movement. The other, opposite case, where the system is unstable, also fails to conform to the conception of an individual, since it significes in essence the progressive incompatibility of parts of the system, leading to its disintegration."

"For this reason, oscillatory systems conform best of all to the conception of an individual as a system which, on the one hand, retains its structure and, on the other hand, is capable of internal movement" [20].

A. S. Kardasheva writes: "In general, only oscillatory systems and processes have a chance for 'survival,' preservation."

"Thus, homeostasis is based on fluctuation, rhythmicity of physiological functions...' rhythm is a means of achieving homeostasis" [12].

T. G. Dichev and K. Ye. Tarasov observed in their book: "Biorhythms turn out to be the principal means of maintaining endogenous homeostasis, the main activity of functional systems of the body and anticipatory reflection of

reality." And further: "Adaptation is characterized by equilibrium and dynamism that change from one to the other. This is, primarily, endogenous equilibrium and coordination of all processes in the body, its homeostasis as stable movement or mobile stability" [11].

H. Hensel believes that "although living organisms do have a certain permissible range of values for a parameter, the rhythmic change in this parameter as a function of time is expressly the mandatory condition for existence. Strict maintenance of the same value of a biologically controlled parameter would lead to disruption of normal vital functions. We can take the circadian rhythm, a vivid manifestation of which is the alternation of wakefulness and sleep, as the best known example" [36].

V. Ye. Sokolov and G. V. Kuznetsov write: "We are justified in referring to the circadian rhythm of animal activity as adaptation, which includes an entire set of special adaptations of the body ... aimed at maintaining the optimum sequence of phases of vital functions of animals in a specific environment" [30].

Thus, in the course of systematic analysis we have arrived at discussion of biological rhythms, starting from the general concept of adaptation as a means of providing for homeostasis. The biological rhythm in question is a vivid manifestation of the laws of dialectics, primarily its law of unity and struggle of opposites. Researchers who work in the field of biorhythmology are coming to this more and more closely and increasingly often.

With reference to the daily movement of plant leaves, E. Buhnning observes that this movement is based "on either antagonistic fluctuations in growth of top and bottom sides of a leaf, or antagonistic fluctuations of turgor within cells of the top and bottom half of the leaf articulation" [3].

K. Tomov [32] formulates well his idea about the essence of biological rhythms: the source and moving force of any development are the unity and struggle of opposites. Hence, there must be alternate dominance of one opposite over the other for movement to occur, otherwise movement would stop. This alternation is manifested by the oscillatory nature of each movement.... All forms of movement of matter, all interactions constitute oscillations and derivatives of oscillations which are based on laws of dialectics: the unity of opposites, change of quantity into quality and vice versa, denial of negation.

In the course of investigation of human circadian rhythms in our country, a definition was formulated for biological rhythm, according to which it is a form of movement of living matter, in which there is objectivization of the unity and struggle of opposites--destruction and creation, which are the basis of self-reproduction.

Such an idea had already occurred to ancient scientists who maintained that anything living in time and space is alive because it contains polarity and rhythm, which give life to the entire universe; for this reason, life signifies rhythm. This idea survived for millenia and has now been taken up as a toool by natural sciences.

Here are a few examples:

"We see rhythm everywhere, everywhere on earth and in the sky ... we always find rhythm in all of the diverse manifestations of life. The life process is always a rhythmic process in some form or other ... we can view the life of our body as a complex fabric of innumerable, extremely diverse rhythms" [25].

"... Rhythms are an inseparable property of living systems and constitute the basis of their organization" [24].

"Rhythm is a universal law of nature" [28].

"Rhythm is one of the most vivid and widespread phenomena. Rhythms are inherent in both phenomena in the inorganic world and biological phenomena" [37].

"Cycles, or rhythms, are a general law of the universe both on the scale of macrospace and as part of the microspace of inanimate matter. For this reason, there is nothing surprising about the fact that cycles are also a dominant feature of living nature" [31].

"Periodicity is just as much a basic feature of life as excitability of living tissues, homeostasis in a biological system or the capacity to adapt to the environment and living conditions. Periodic changes also involve these basic distinctions. Excitability of all living tissues fluctuates in accordance with the rhythms inherent in a biological system. The conception of homeostasis ... signifies stability of the range, in which periodic fluctuations of the state of an organism occur...." [27].

There is no need for more examples that assert the prevalence of the conception of rhythmicity as the basic property of life. In the light of our topic, it is very important to analyze this rhythmicity in terms of dialectics.

The link between rhythm and unity of opposites is confirmed by an enormous amount of experimental material. But this is only a general thesis, analysis of which reveals to us that beyond what we call the rhythm of an organism is a "complex fabric of innumerable, extremely diverse rhythms," with periods lasting from milliseconds to several years. Dialectics maintains that there is always a main, leading contradiction in the complex fabric of diverse contradictions. In our times, there have been descriptions of many contradictions inherent to a complex organism, in particular, man. We shall furnish some of them below.

Beta cells of pancreatic islets produce insulin; alpha cells of the same gland produce hyperglycemic hormone; thrombocytes and mast cells are antagonists in the blood-clotting system; the hypertensive effect of granular cells of the juxtamedullary system of the kidneys and hypotensive effect of interstitial cells of the medullary layer of the kidneys; cells of the adrenal glomerular zone that stimulate an inflammatory reaction and cells of the fascicular zone that depress it; basophils of the hypophysis that activate growth and maturation of ovarian follicles and lutein cells of the corpus luteum that inhibit these processes; enzyme modulators that increase and

decrease enzyme activity; neuropeptide particles of the hormone vasopressin which fix information in the brain and neuropeptide particles of the hormone oxytocin that erase it.

Analysis of these contradictions shows that we have every justification to single out the contradiction between destruction and creation, that emerges in the form of rhythm, as the main one. Claude Bernard had already written: "We divide signs of life into two major categories: wearing out, or destruction, and creation. Everything that happens in a living being is referable to one or the other of these types, and life is characterized by a connection or linkage of these two categories of phenomena. We feel that this is the best classification of life of all those that could be suggested in general physiology. It is the expression of life in that it contains what is extensive and the most precise. It applies to all living things without exception..." (quoted by D. S. Sarkisov [26]).

Circadian rhythms hold the leading place in the system of life rhythms. Examination of the phenomenon of circadian rhythms reveals the following:

> The basic states of the body, sleep and wakefulness, are subject to circadian fluctuations.
>
> Sensitivity of the body to various exogenous factors fluctuates in a circadian rhythm.
>
> Coordination of circadian rhythms is a mandatory prerequisite for the welfare of an organism, its health and work capacity.
>
> Circadian rhythms have been demonstrated in all representatives of the animal kingdom, ranging from protozoans to man, and on all levels of organization, from cellular processes to behavior [40].
>
> Circadian rhythms are notable for amazingly small deviations of period length from the mean value with free course of rhythms [24].

These theses enable us to attribute to circadian rhythms the role of the main element in the integral system of the organism, the common starting point that is the basis for combining all fragments of the organism into a single whole. "The sole rhythm of a given system emerges as a feature that is indicative of the functional unity of the system" [12]. This rhythm is undoubtedly circadian, a form of communication of all fragments of the organism, a communication that has elements of universality and necessity. Indeed, circadian rhythms have been recorded in all cases where a record was taken. The universality trait of circadian rhythms is a firmly established fact. Health and work capacity are based on circadian rhythms. Some degree of synchronization of circadian rhythms is necessary to preserve the welfare of an organism.

As we know, connections with signs of universality and necessity are referable to laws, which entitles us to refer to the circadian nature of rhythms as a law, the action of which is provided by vital functions of the organism as a whole.

Thus, analysis of the adaptation problem logically leads to determination of its relationship to the problem of homeostasis and, through the latter, to the problem of biological rhythms and, in particular, circadian rhythms which inherently have the features of universality and necessity.

Movement of our thoughts over the complex and sometimes convoluted relations between phenomena and processes in the world around us turns out to be fascinating and fruitful. But whenever dialectics remains as the compass for this route, sooner or later we gain some of nature's mysteries, untying successive knots in the inexhaustible network of correlations inherent in it. And, there is no question but that F. Engels was right when, in the most general definition of dialectics, he attributed to it the rank of science dealing with universal relationship. Not the science of universal links, which would not have ruled out ideas of separateness, but science of universal relationship. Such an approach to investigation of any problem in any discipline eliminates the danger of scientific "dead-ends," "definitive" solutions to some scientific problem or other, since in a system of universal relationship each step forward sheds new light on already achieved conquests of science that had appeared entirely disclosed, since their meaning had often been examined and continues to be examined within the narrow range of achieved understanding of the scope of the relationship, in which they were included.

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RADIO-FREQUENCY ELECTROMAGNETIC RADIATION: RADIATION SAFETY

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[Article by B. I. Davydov]

[English abstract from source] Existing safety standards for electromagnetic radiation in the radio frequency range, including microwave radiation, adopted in the USSR, Great Britain, Poland, Czechoslovakia, USA, Canada, FRG and recommended by IRPA/INIRC are described. It is porposed to use the value 0.4 W/kg as the basic value of an absorbed dose rate which corresponds to the energy flux density 100 W/m^2 for frequencies over 2 GHz. The concepts of an effective dose rate and effective dose are discussed. Various questions of how to provide safety of those working with electromagnetic radiations are considered.

[Text] At the present time there are practical applications for virtually all ranges of radio-frequency radiation (from a few kHz to hundreds of GHz). In particular, the power of radar systems (RS), which operate mainly in the SHF range, is increasing and, according to some data, by 10-30 times per decade. In the future, the RS power for communication with satellites will reach a few terawatts. Recently, there has been interest in critically low frequencies (CLF), at which superdistant communication is possible [20], and critically high frequencies (CHF): RS with high resolution, radio-relay communication lines with spacecraft, etc. [9].

According to an international convention, the entire spectrum of nonionizing electromagnetic energy is divided into 12 groups of frequencies, from 0 Hz (or stationary electric field) to $3 \cdot 10^{12}$ Hz (3 THz)(Footnote 1)(1 THz = 10^{12} Hz). Table 1 lists the classification of EMR (Footnote 2)(Hereafter, EMR will refer to radio-wave radiation, including microwaves). The 9th-11th ranges are referable to microwaves. In the Soviet literature they are combined in one range of SHF radiation [11].

A system of radiation safety is the set of biomedical and engineering-technical methods, equipment and measures called upon to provide optimum conditions for the work of professional workers, life, health and social welfare of the public.

Table 1.
Classification of EMR

Frequency range No	Abbreviation		Frequency, f	Wavelength, λ
	English	Russian		
5	LF	NCh	30 - 300 kHz	10 - 1 км
6	MF	Sch	300 - 3000kHz	1 - 0,1 км
7	HF	VCh	3 - 30 MHz	100 - 10 м
8	VHF	OVCh	30 - 300 MHz	10 - 1 м
9	UHF	UVCh	300 - 300 MHz	1 - 0,1 м
10	SHF	SVCh	3 - 30 GHz	10 - 1 см
11	EHF	KVCh	30 - 300 GHz	10 - 1 мм

Note: LF, MF, HF, VHF, UHF, SHF and EHF refer to low, medium, high, very high, ultrahigh, super high and extremely high frequencies, respectively.

Failure to adhere to safety practices, particularly when working with an RS, could lead to undesirable somatic consequences [32] and psychological trauma [28]. The true somatic harm of EMR [electromagnetic radiation] may be considerably less than the psychological sequelae due to hyperbolization of the hazard of EMR. Suffice it to refer to some reports published a few years ago in the press, in which there was hyperbolization of the hazard of EMR (critical analysis of these reports is made in [5, 25, 28]) without proper critical analysis of the hygienic situation.

With all the difficulty of dosimetry, vagueness of spatial distribution of energy and difficulty of finding an appropriate biological equivalent, individual and group protection against EMR is much simpler, better available and cheaper than protection against ionizing radiation [29]. We can agree with this only if the hazard of this factor is not exaggerated. In providing for radiation safety, the following questions must be answered: at what dose levels should there be protection and what should be protected (the whole body or certain sections or organs), how one should be protected and, finally, what is the efficacy of protection. In general, the basic biomedical and engineering directions of investigations of EMR for hygienic purposes amount to the following:

Biological assessment of EMR (qualitative: harmful or not harmful).

Search for general guidelines (criteria) that would permit quantitative evaluation of dose-effect (answer to the question of extent of harm).

Determination of experimentally and theoretically reliable, socially warranted EMR levels for the public and "professionals" (assess the hazard to large and small groups of people).

Search for rational (adequate, scientifically validated) means of prevention and protection, depending on extent of harm to different population groups.

Validation of neeed for protective equipment, medical prevention and treatment.

Performance of periodic epidemiological (sanitary and hygienic) inspection of populated areas, enterprises and other areas of contact between people and EMR (evaluation of existing measures

for radiation safety); strict scientific isolation of the "deleteriousness" of the studied EMR factor from many others associated with it.

Implementation of publicity about the social benefit and explanation of range of EMR harmfulness.

In practice, all of these aspects are resolved simultaneously. Many of them are virtually solved, but in spite of this researchers are returning (from new vantage points) to the search for answers to a number of questions in old established positions. In recent times, EMR standards have been particularly subjected to revision. There are several rather comprehensive works dealing with validation of safety standards when working with EMR. However, there is still no agreement on this score [12, 17, 27, 31]. When properly validated, they not only permit preservation of human health, but a rather reliable level of work capacity (ergonomicity of standards), and make it possible to avoid unnecessary psychological trauma and, ultimately, bring a benefit to society.

1. Units of Measurement

Questions related to field dosimetry, theoretical and experimental evaluation of electromagnetic field (EMF) energy absorbed by the body were discussed in detail in several articles [7, 18, 24]. According to the latest recommendations of the International Committee on Nonionizing Radiation of the International Association for Radiation Protection (IRPA/INIRC), specific absorption rate (SAR) or specific absorption rate per unit body weight is taken as the basic dosimetric value of EMF energy absorbed by the body for frequencies under 10 MHz [18, 24].

In SI [international system of units] units, SAR is expressed in watts per kg (W/kg). SAR can reflect both the mean absorption rate for the whole body or part of the body, for both a specific time interval or one count. SAR can be calculated theoretically (which in itself is a difficult task) or estimated experimentally.

For the range of frequencies under 10 MHz, effective voltage of the electric field (E_{ef}) and effective voltage of the magnetic field (H_{ef}) are used as the main dosimetric parameters. In SI, E_{ef} and H_{ef} are expressed in volts per meter and amperes per meter, respectively.

Rate density or energy flux density (EFD) emerges as a derivative parameter reflecting energy of the field in the absence of an irradiated object. In the SI, EFD is expressed in watts per square meter.

In the far zone there is a rather universal link between EFD, E and H:

$$I = E^2/120\pi - 120\pi \cdot H^2, \quad (1)$$

$$H = E/120\pi \quad (2)$$

where I is expressed in W/m^2, E in V/m and H in A/m.

In the close-range field and complex, multiple fields, both electric and magnetic components of EMF must be measured. For frequencies under 10 MHz, the EFD values given in the standards are arbitrary.

2. Standards of Different Countries

The greatest attention to EMR and standard-setting for it is given in the USSR, PNR [Polish People's Republic], CSSR, United States, England and Canada. First of all, one should make a distinction between standards for the public and for individuals working with EMR sources. Soviet investigators of hygiene of inhabited areas [6, 14] devote attention to EMR standards. At the same time, in the United States, the minimum threshold level for professionals was previously considered as a permissible level for the public.

Table 2.
Maximum permissible levels of EMR in the radiofrequency range for the public in different countries [6, 8, 14, 16, 22, 24, 26, 30]

Country	f, MHz	I, W·м$^{-2}$	E, V·м$^{-1}$
USSR	0,03–0,3	1	20
	0,3–3	0,25	10
	3–30	0,01	4
	30–300	0,01	2
	300–300 000	0,05 (0,15–0,25)*	4(8–10)*
PNR	0,1–10	1	20
	10–300	0,12	7
	300–300 000	0,1(1)**	6(20)**
United States	0,01–300 000	10	60
	0,01–300000***	0,5	11
England (NCRP recommendations)	0,003–3	1000	600
	3–30	$900/f^2$	$1800/f$
	30–300	10	60
	300–1500	$f/30$	$3,5\sqrt{f}$
	1500–300 000	50	140
IRPA/INIRC (recommendations)****	0,1–1	20	87
	>1–10	$20/f$	$87/f^{1/2}$
	>10–400	2	27,5
	>400–2000	$f/200$	$1,375 \cdot f^{1/2}$
	>2000–300 000	10	60

*In parentheses, temporary standards for pulsed-intermittent exposure to surveillance RS in ranges of 10, 23 and 35 cm.

**In parentheses, intermittent (scanning) irradiation.

***Special suggestions (New York Health Department) [30].

****International Committee on Nonionizing Radiation of International Association for Radiological Protection [24].

NCRP--National Committee for Radiological Protection

Table 3.
Standard levels of continuous and intermittent EMR exposure for professional activities (based on 8-h work) in the USSR, PNR and CSSR [3, 12, 16, 26]

Country	f, MHz	I, W/м^2	E, V/м
USSR	0,06–3	7	50
	3–30	1	20
	30–50	0,25	10
	50–300	0,06	5
	300–300 000*	0,25 (2,5)	10 (30)
PNR	0,1–10**	12	70
	10–300***	1	20
	300–300 000****	2 (10)	30 (60)
CSSR	0,1–30	7	50
	30–300	0,3	10
	300–300 000	0,25 (0,1)	10 (7)

Note: Intermittent (i) or pulsed field in parentheses.

* $I(r) = 2/I$; $I(r) = 20/I$ (i).
** $I(r) = 560/E$ ($E \leq 1000$ V/м).
*** $I(r) = 3200/E^2$ ($E \leq 300$ V/м).
**** $I(r) = 32/I^2$; $I(r) = 800/I^2$ (i) ($I \leq 100$ W/м^2).

Table 2 lists maximum permissible EMR levels proposed as standards by the Kiev Scientific Research Institute of General and Communal Hygiene [6, 14] and the standards of several other countries [15, 17, 21, 26]. As can be seen in Table 2, the permissible level of microwave radiation for the public was increased by 5 times (the earlier proposal of Z. Gordon et al. [2] corresponded to 1 μW/cm^2). At the present time, temporary EFD levels have been proposed for the public with respect to airport surveillance RS. A maximum permissible value of 1 mW/cm^2 was adopted in the United States and Canada [15].

The British National Commission on Radiological Protection (NCRP) [22] has suggested intensity of infrared radiation of the sun, to which man is exposed, as a criterion for determining the permissible level of exposure for the public, and it recommended permissible EMR levels for the public, including children (see Table 2). Table 2 also lists the recommendations of IRPA/INIRC.

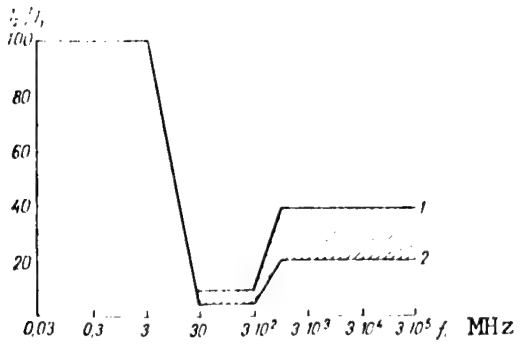
More complicated and more differentiated standards were elaborated for industrial conditions. Table 3 lists standards for labor safety when working with radiofrequency EMR, which were adopted in the USSR, PNR and CSSR [3, 12, 16, 26]. The adoption of GOST 12.1.006-84 led to some increase in permissible EFD for frequences of 0.3-300 GHz. However, they are still lower for the same exposure time than the standards adopted even in PNR [16, 26], and considerably lower than standards of the United States, England, Canada and FRG [17, 21, 27, 31]. At the same time, in their latest suggestions the NCRP of these countries lowered EFD levels to 1 mW/cm^2 for resonance frequencies (Table 4).

Table 4. Proposed safety standards for EMR (constant and intermittent exposure) in radio-frequency range in the United States, England, Canada and FRG (8-h work day) [17, 21, 22, 24, 27]

Country	f, MHz	I, $W \cdot м^{-2}$	E, $V \cdot м^{-1}$	H, $A \cdot м^{-1}$
United States*	0,3—3	1000	600	1,6
	3—30	$9000/f$	$1800/f$	$5/f$
	30—300	10	60	0,16
	300—1 500	$f/30$	3,5	$9{,}4 \cdot 10^{-3} \sqrt{f}$
	1 500—100 000	50	340	0,36
England	0,03—3	1000	600	1,6
	3—30	$9000/f^2$	$1800/f$	$5/f$
	30—100	10	60	0,16
	100—1 000	$f/10$**	6	$0{,}006 \sqrt{f}$
	1 000—300 000	100**	200	0,5
Canada	10—1 000	10	60	0,16
	1 000—300 000	50***	140	0,36
FRG	0,03—2	—	1500	$7{,}5/f$
	2—30	—	$3000/f$	$7{,}5/f$
	30—3 000	25	100	0,25
	3 000—12 000	$25f/3000$	$100 \sqrt{f/3000}$	$0{,}25 \sqrt{f/3000}$
	12 000—3 000 000	100	200	0,5
IRPA/INIRC	0,1—1	100	194	0,51
	>1—10	$100/f$	$194/f^{1/2}$	$0{,}51/f^{1/2}$
	>10—400	10	61	0,16
	>400—2 000	$f/40$	$3 \cdot f^{1/2}$	$0{,}008 \cdot f^{1/2}$
	>2 000—300 000	50	137	0,36

*Permissible dose 144 J/kg/0.1 h (0.4 W/kg/0.1 h).
**Maximum of 500 W/m^2 for no more than 1 min.
***Maximum of 250 W/m^2 for no more than 1 min.

Moreover, some American researchers [30] propose even more rigid standards for some parts of the country: 0.5 mW/cm^2 for professionals, 0.05 mW/cm^2 for the public. We cannot agree entirely with this trend toward lowering tolerable EMR levels for professionals and, unquestionably, one should support the tendency toward setting rigid standards for the public. According to the



Correlation between permissible EFD levels (for 8-h work day) in two groups of countries: USSR, PNR, CSSR and United States, England, Canada

- I_1) mean permissible EFD in the USSR, PNR and CSSR
- I_2) same in the United States, England, Canada
- 1) as compared to English standard
- 2) as compared to standards of the United States and Canada

recommendations of the WHO and International Committee on Radiological Protection, EFD of 0.1-1 mW/cm^2 are sufficiently safe in the case of long-term exposure for the entire range of frequencies.

The Figure shows that the EFD differences at different frequences between values for the USSR, PNR and CSSR, on the one hand, and the United States, England, Canada and FRG, on the other hand, present the least differences in the range of resonance frequencies (30-300 MHz). To plot this curve, the appropriate approximations of tolerable EFD (8-h work day) for the two groups of countries were made in frequency ranges of 0.03-3, 3-30, 30-300, 300-1500-300,000 MHz. Conversion of intensity (E) to EFD (1) was made according to [1].

3. Some Suggestions for Changing Standards

At the present time, Soviet standards assure safety thanks to low levels of EMR to which working personnel and the public are exposed. In the future, it will inevitably be necessary to revise the standards, yet this is undesirable from the psychological point of view. It is necessary to strictly validate standards, regardless of social and technical considerations.

At the present time, standards are recommended in the United States, England and certain other countries that are related to radiation frequency. The lowest EFD, 1 mW/cm^2, proposed by these countries for resonance conditions could hardly be called high, although it could be lowered to 0.5 mW/cm^2 (0.2 W/kg for resonance conditions), but not any lower. This level is within the range of fluctuation of human energy expenditure at rest. As for the level of 10 mW/cm^2 (0.4 W/kg) proposed for frequencies in excess of 1000 MHz by the British NCRP [22] and URPA/INIRC [24] for "professionals," as shown by our analysis [5] it is 1/10th the natural risk level, which is 0.1%. If we consider that primarily airport personnel and crews of aircraft and helicopters are exposed to EMR (risk of death is 2% [1]), the standard of 0.4 W/kg does not seem so high.

Previously [4, 5], views were advanced concerning establishment of tolerable levels for the microwave range ($f \geq 2$ GHz) based on the concept of risk. EFD of 100 mW/cm^2, or 4 W/kg (SAR 0.04 W/kg per 1 mW/cm^2 [18]) was proposed as the base value in setting the safety standard, and with consideration of the safety factor taken as 10-10 mW/cm^2, or 0.4 W/kg, for frequencies in excess of 2 GHz.

Validation of acceptable or permissible EMR levels was based on three principles: criterion of risk, thermal effects and absence of accumulation with SAR of 4 W/kg or less [4, 5]. The British NCRP [22], using a different ideology of validation, also recommends 4 W/kg (with a safety factor of 10-0.4 W/kg) as the base value. The NCRP of that country proposes that 30-100 MHz be considered the range of resonance frequencies, whereas ANSI (United States), cites 30-300 MHz. The following are proposed as transitional ranges, where EFD increases proportionately to frequency: 100-1000 MHz ($I = f/10$) and 300-1500 MHz ($I = f/30$). If we accept 0.04-0.2 $(W \cdot kg^{-1})/(mW \cdot cm^{-2})$ as the extreme SAR and 0.4 W/kg as the base value for frequencies in excess of 1500 MHz, EFD in the transitional range of 300-1500 MHz would be expressed as

$$I = f/15 \qquad (3)$$

where I is given in watts/m^2 and f in megahertz. The range of 30-300 MHz can be considered as resonance, where EFD does not depend on frequency and constitutes 20 W/m^2. EFD as a function of exposure time is expressed by an exponential function [5]:

$$\log I = 2.25 - 0.7 \log t_m \quad (f \geqslant 1500 \text{ MHz}) \qquad (4)$$

where t_m is time (in minutes) and I is EFD (in mW/cm^2).

The ratio, $I^2 \cdot t = \text{const}$ (used in the PNR standard [16, 26]) is more convenient for calculations; it offers additional safety to the standard. Then (4) would be:

$$I = 110\sqrt{t_h} \qquad (5)$$

where t_h is exposure time (in hours) and I is EFD (in W/m^2).

For frequencies of 300-1500 MHz, equations (3) and (5) can be combined:

$$I = (100\sqrt{t_h})/(1500/f);\ 0.1 < t_h < 1$$

With $f \geqslant 1500$ MHz the second term in the equation always equals 1.

One can accept as EFD of justified risk a value of 500 W/m^2 for frequencies in excess of 1500 MHz and 100 W/m^2 for frequencies of 30-300 MHz. A level of 5000 W/m^2 for nonresonance conditions and 1000 W/m^2 for resonance conditions (20 W/kg) would be critical, and it could elicit extremely undesirable consequences (at a risk level of 0.1%) after brief (no more than 0.1 h) exposure.

4. Dose Principle: Effective Rate, Effective Dose

There are major difficulties in evaluating EMR doses, although such an approach is very tempting. While it is possible to translate absorbed energy into the corresponding thermal effect expressed in joules in the case of acute and short-term exposure, in the case of chronic exposure or delivery of divided doses of radiation this is feasible only if one believes that a residual lesion remains after each portion of irradiation. The latter is mandatory, since only then could one determine effective dosage, as is done for ionizing

radiation. Hirsh was the first to try to draw a dose analogy between the two ranges of electromagnetic energy in 1965. B. Minin assembled information on this score [10]. As shown by analysis, the bottom threshold of dose rate at which dosage should be evaluated by other criteria was never given. B. M. Savinet al. (quoted in [10]) were correct in indicating the range of EFD when using the dose approach: 1-50 mW/cm^2 for the microwave range. We cannot fail to concur with this. Even greater difficulties arise in assessing EMR doses in the case of pulsed, divided dose or protracted exposure. In theory, we should have assessed effective irradiation dose per count, rather than SAR averaged in time. Any averaging of dose without consideration of dose rate yields distortedestimates of biological effectiveness of EMR. In radiobiology of ionizing radiation, the role of dose rate is distinctly viewed in such systems as hemopoiesis, the gastrointestinal tract and the central nervous system. There is every reason to believe that the same may be observed with exposure to EMR. For this reason, consideration of "peak" exposure is very important (particularly when assessing damage to the central nervous system). Hence, dosimeters must take into consideration both the maximum "peak" EFD (SAR is better) and exposure time, as well as the integral average value over a specific period of time. Apparently, minimum averaging time must be equal to or less than the rate of recovery of the selected physiological function.

In order to assess the effective dose, one must take into consideration the effect of factors other than the quality factors inherent in EMR (frequency, grounding, reflective surfaces). We refer, first of all, to the thermal environment and ionizing radiation. According to our data [5], ionizing radiation can enhance the biological effect of EMR by about 2 times. Tell and Harlen [31], who used the formulas of Givoni and Goldman [19], which take into considerations parameters such as air temperature, vapor pressure, wind velocity and clothing, obtained changes in body temperature as a function of EFD for resonance conditions (75 MHz). These authors demonstrated that virtually up to 20 mW/cm^2, rectal temperature does not change by more than 1°C under the following ambient conditions: air temperature 25°C, pressure of vapor in air 12 mm Hg, relative humidity 50%, wind velocity 0.13 m/s; subject wearing light clothing at rest. At temperatures in excess of 25°C effective dose rate should be reduced to 1/2. GOST 12.1.006-76 recommends lowering EFD to 1/10 at a temperature of 28°C. In GOST 12.1.006-84 [3], this recommendation was eliminated for good cause, since we are dealing with EFD of less than 10 W/m^2. An additional physical burden also aggravates the heat balance of man exposed to EMR. Intensive work is undesirable with SAR in excess of 4 W/kg (10 mW/cm^2 for f>1 GHz). Core temperature can be used as a criterion of total-body and long-term irradiation only for nonresonance frequences and EFD that is not too high, no more than 10 mW/cm^2. With increase in dose rate under resonance conditions, there is local overheating of tissues without a corresponding elevation of rectal temperature. An analogous situation may occur with intensive and brief local irradiation of the head [5]. If we also consider the effect of reflective surfaces, grounding of the subject and other factors, the effective dose rate could increase 1000-fold [7, 18]. We also cannot fail to consider the fact that, in the case of resonance frequencies, the wavelength for man would be about 4 m. Thus, an operator would usually be situated in the close-range zone of the EMR source when at work, in the zone of an unformed wave, where dosimetry presents great difficulties and evaluation of local SAR is rather vague.

It is hardly desirable to offer a single standard for professionals with consideration of all these factors. They must be considered in each specific case, and the standard must conform to a particular effective dose. By adding the concept of irradiation quality factor (η), which is defined as the ratio of intensity of standard irradiation that generates a specific SAR in a biological system to intensity of this irradiation eliciting the same SAR, one can move on to the concept of effective intensity of irradiation (I_e), which is found from the equation, $I_e = I \cdot \eta_\eta$, where I is intensity of radiation. One can take a frequency of 2.4 GHz (or >300 MHz) as standard radiation. Analysis of conditions of formation of SAR revealed an overt relationship between quality factor and frequency in free space (η_1), presence of reflective surfaces in the vicinity (η_2), electric contact with the ground (η_3), ionizing radiation (η_4), elevated temperature (η_5), etc.

With consideration of these functions for three types of polarization and factors η_{1-3}, one can write down:

$$I_e = \eta_1(\bar{E}, \bar{K}, \bar{H}) \cdot \eta_2(\bar{E}, \bar{K}, \bar{H}) \times \\ \times \eta_3(\bar{E}, \bar{K}, \bar{H}) \cdot I,$$

where η(E, K, H) means that the factor is a function of type of polarization.

At frequencies of 1-30 MHz, $\eta_1 = 0.5$, $\eta_2 = 1$, $\eta_3 = 10$; at frequencies of 30-300 MHz, the figures are 8, 25 and 5, respectively [7]. These factors are considerably lower for other polarizations. At frequencies above 300 MHz, η_1 and η_3 equal 1, whereas η_2 is determined from conditions of geometric optics.

For example, exposure of man to radiation with intensity of 10 mW/cm^2 at a frequency of 2.4 GHz in free space generates the same SAR as exposure at a frequency of 70 MHz with E polarization, grounding, presence of reflective surfaces and intensity of 0.01 mW/cm^2. This is the maximum irradiation quality of all the possible variants. Of course, under controlled conditions, it is desirable to assess in each case the irradiation conditions, rather than to have a standard that considers all of the most unusual exposure conditions. It should be borne in mind that the range of frequencies, at which such a marked enhancement of effectiveness of EMR is possible, is not so great when expressed as a percentage, no more than 0.1% in the frequency range of 1 MHz to 300 GHz.

Evaluation of the hazard of the radio-frequency spectrum of EMR can be made by the method of competing frequencies or bands [7]. In the general case, in the presence of a series of m competing frequencies, the intensity of which is measured in V/m and a series of k frequencies, the intensity of which is measured in W/cm^2, irradiation may be considered safe if the following condition is satisfied:

$$\sum_{i=1}^{m} \left(\frac{E_i}{E_{i,\,\mathrm{per}}}\right)^2 + \sum_{i=1}^{k} \left(\frac{I_i}{I_{i,\mathrm{per}}}\right) \leqslant 1,$$

where intensity E_i is voltage of electric component of the field for the ith frequency band; I_i is intensity of the ith frequency band; $E_{i,\mathrm{per}}$ is the required maximum permissible intensity at the ith frequency, $I_{i,\mathrm{per}}$ is regulated maximum permissible intensity of ith frequency.

5. Some Organizational Aspects of Radiation Safety

Perhaps the most complicated aspect of protection against EMR is referable to organizational measures. They include an extremely broad range of problems ranging from providing dosimeters to technical personnel to determination of perquisites related to the harmfulness. The latter is a prerogative, not only of public health workers but administrative and finance agencies. The most complex aspect of the safety problem is to define perquisites by assessing the degree of harm. At the present time, there are no clearcut criteria or quantitative factors for setting privileges. In the triad of factor, harmfulness and perquisites, the latter has been worked on the least. Recently, the International Committee on Radiological Protection [23] introduced in the place of the concept of "risk" (as the quantitative analogue of harmfulness) that of "detriment," defining it as an overall concept that includes actual loss of health and any other elements of detriment (some of which may be subjective). It is difficult to maintain that absolutely indisputable criteria will be found to assess the "cost of detriment" or "privilege for harmfulness." We are dealing here with a set of social and psychological conventionalities. Further discusssion of this complex issue would lead to the necessity of touching upon philosophical, sociopolitical and moral-ethical aspects of this problem. However, one thing is unquestionable, their realization according to many factors of work is possible only in socialist countries.

One should include in organizational problems primarily wise (from the standpoint of safety) location of emitting systems (RS, radioelectronic communications, etc.), as well as residential buildings in relation to EMR sources, organization of group and individual protection, dosimetric monitoring. This aspect of protection is the most difficult, since the conditions for locating sources of emission are sometimes motivated by considerations that are more important to society and the nation than hygienic requirements. As a rule, they are socially warranted. The task for physicians is to find optimum solutions. The concept of "absolute harmlessness" [1] is just as illogical as the concept of "ideal protection."

Organizational measures should also include the process of adopting the appropriate standards.

As applied to working conditions, we can also list some organizational guidelines for radiation safety:

> Organization of work schedule so that there is minimal duration of contact with EMR.
>
> Organization of work place, so that contact with EMR occurs only when necessary to the job; perform only what is required by the engineering or work process; preclude the influence of reflective surfaces and operator grounding.
>
> Organizational work during emergency situations. Clearcut regulations as to time and space of operations. Accidents may be related to many factors: EMR and ionizing radiation, electrically

dangerous situations, etc. In this case, one must choose the principal factor. In particular, EMR is the least dangerous of these three factors.

Professionals (pilots, engineers, operators, etc.) must have an absolutely clear idea about the harmful and harmless limits, regardless of whether they receive benefits due to the harm or not. For this, there must be clear and objective information about the absolutely proven effects of EMR. Publicity about the social significance of sources that emit radio-frequency radiation to society and possible biological effects of EMR must also be aired for the public.

In assessing the extent of harm of EMR (particularly in the SHF range), hygienists usually try to find the radiation maximum, sometimes even where there are no people at any time. This raises the exposure level fallaciously. One could try to justify this with the unwise desire to exaggerate the hazard of EMF. It is necessary to take into consideration not only the level of irradiation, but probability of exposure to some dose or other of either the entire body or parts of it (for example, the hand of a mechanic who repairs equipment or the head of an operator of various radio-frequency installations. The success of protective measures must be checked by epidemiological observations and evaluated by economic indicators.

Such propaganda should be practiced with regard to all factors. It is necessary to relate the "harm" of EMR to other factors and, in particular, such as ionizing radiation, chemical pollution of the environment, high temperatures, noise.

Only epidemiological observations are the final judge of all proposed measures for radiation safety. This is a complicated issue and should be discussed separately.

Questions of radiation safety are related the most to economics. Expenditure of manpower and resources, for example to implement protective measures (industry, installation, operation), sometimes exceeds by many times the expenses for taking readings, conducting scientific research and preparing forecasts. Quite often these expenses are comparable to the cost of the EMR sources themselves. Moreover, introduction of methods and means of protection usually has an adverse influence on ergonomic and economic indicators of the developed EMR installations. Standards have a direct effect on the tactics of preventive and protective measures.

G. I. Sidorenko et al. stress that unjustifiably rigid hygienic standards could lead to unnecessary economic loss [13]. For this reason, the standards must be scientifically strictly validated, since every "extra" milliwatt they indicate costs the government dearly.

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UDC: 612.014.461.3+612.015.31:541.135]:519.86

MATHEMATICAL MODELS OF FLUID-ELECTROLYTE METABOLISM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 2, Mar-Apr 86 (manuscript received 3 Feb 84) pp 24-27

[Article by A. I. Grigoryev and V. V. Verigo]

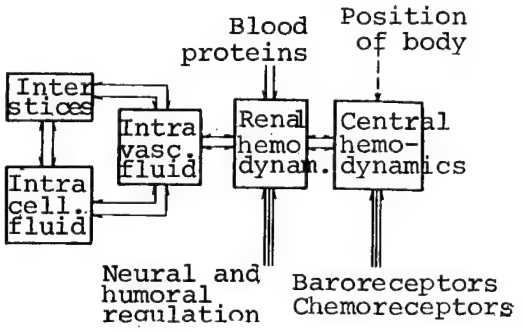
[English abstract from source] This paper describes mathematical modeling of fluid-electrolyte metabolism and fluid homeostasis in real and simulated microgravity. At the first stage physiological reactions to provocative tests were simulated. The assumptions made yielded satisfactory results, particularly with respect to the excretion of the most important electrolytes in different time intervals of bed rest and recovery. The development of models of fluid homeostasis, taking into consideration tissue elasticity and plasticity and fluid buffering capacity, is discussed.

[Text] The system of fluid-electrolyte metabolism plays an important part in the process of human adaptation to spaceflight conditions [4, 6, 11]. At the present time there are some pressing tasks, such as investigation of dynamics of electrolyte concentration in blood plasma and their excretion, investigation of systems of regulating ion and fluid transport, analysis of possible mechanisms of change in fluid and electrolyte metabolism. An effective solution of these problems will help both with respect to better understanding of the routes of establishment of a new homeostatic state during flight and search for the methods and means of controlling this process.

In such investigations, mathematical modeling of processes of fluid-electrolyte metabolism may be quite useful. At the present time, we know of several works in this direction, among which we should single out the model of circulation of A. C. Guyton et al. [9], which determined many of the subsequent directions of investigation. The first studies dealing with modeling of fluid-electrolyte metabolism in the Soviet Union [3] were concered with models of processes in different segments of the nephron. Analysis of stabilization of volumetric and osmotic parameters with intake of diuretics or mineral water was made in [1] by a team of authors. Simulation of processes of fluid-electrolyte metabolism under extreme conditions was effected at the Institute of Biomedical Problems--IMBP--of the USSR Ministry of Health starting in 1977.

However, the modeling method can and should be used more extensively. The effect of its broader use may be rapid evaluation of the quantitative and qualitative reactions of functional systems to various combinations of exogenous factors by means of computers, verification of hypothesis of mechanisms, that are still not entirely clear, of regulating fluid-electrolyte metabolism and possibility of evaluating parameters that are difficult to measure. The task of simulating the reaction of the system of fluid-electrolyte metabolism to functional load tests was formulated as the first stage of development and practical use of the model.

The diagram illustrates the general structure of the variant that was developed. In preparing the model, established physiological conceptions described previously were used [2, 5, 7, 8]. Rather extensive use was made of equations in appropriate units of the model [9] to describe the internal structure of the units, since it is based on vast experimental material and, in a number of situations, was found to have satisfactory efficiency, taking into consideration in the first approximation the basic effects related to homeostasis of fluid and sodium. However, already at the first stage of investigation it became necessary to make comprehensive corrections and additions to it.



Addition to the model of equations that take into consideration the transport of bivalent calcium and magnesium cations was an important modification; it was assumed that the rate of filtration must be proportionate to their base concentrations in plasma. With respect to rate of reabsorption, it was assumed that it depends on concentrations of the bivalent cations, as well as osmotic concentration of plasma, determined mainly by the concentrations of sodium and chlorine. In accordance with [7], it was assumed that absolute reabsorption of calcium and magnesium is limited, and normally the reabsorption rates are relatively close to their maximum values.

The time constant of change in reabsorption rate in response to change in osmosity of plasma was considered to be relatively short (about 3 min), whereas selective regulation of ion composition with change in concentrations of calcium and magnesium was effected by means of slower change in reabsorption rates (time constant about 1 h).

At the present time, development of the model of potassium transport cannot be considered entirely finished. Perhaps, even with a rather approximate description of this process, it would be necessary to consider not only afferent and central mechanisms of its regulation, but the differential role of different segments of the nephrone, as well as redistribution of blood flow among the different vascualr regions of the kidney.

In the course of working on the model, it was deemed expedient to consider the effect of activation of interstitial volumoreceptors due to ADH [antidiuretic hormone] production and dependence of the latter on osmolarity

of plasma as defined by the contribution of each electrolyte considered. In addition, it was necessary to define expressions for reabsorption of fluid and sodium, consider the lag in the chain of regulation of preglomerular resistance according to filtration rate, introduce links that determine, in accordance with the myogenic hypothesis, the mechanism of self-regulation that provides for the relative stability of renal blood flow and filtration rate over a rather wide range of values for mean arterial pressure (80-120 mm Hg), as well as to make several other modifications. Definition of the numerical values of structural parameters of the model, which was done either by means of formal identification algorithms or simulation search of experimental data, was a rather important phase of the work.

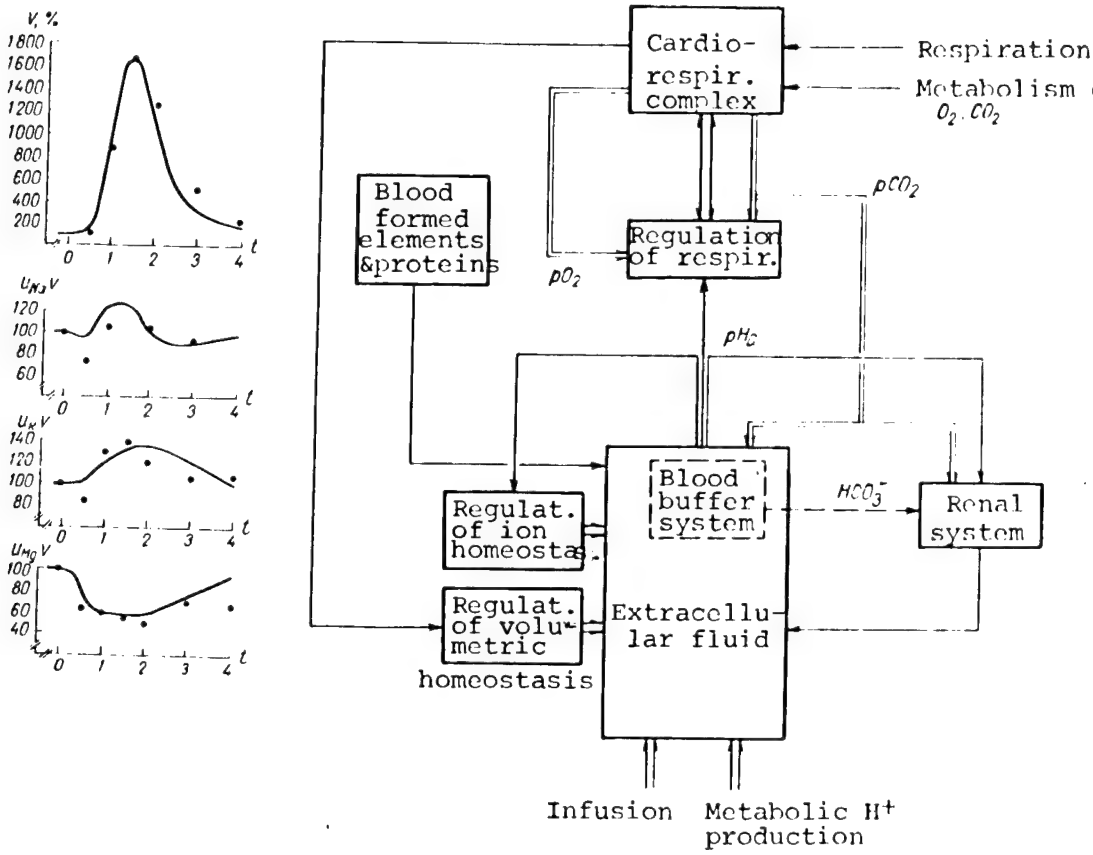


Figure 1. Model of processes of fluid and electrolyte transport during functional test. The curves are functions obtained on the model and the dots are experimental data

Some of the results of calculations made using the model are illustrated in Figure 1, which shows the characteristics of the process of fluid and electrolyte transport during a functional test. A comparison of the curve obtained from the mathematical model to experimental data shows that it is quite adequate to phenomena observed in reality.

Figure 2 illustrates the dynamics of sodium excretion after a 2% water test on the 2d day of hypokinesia and on the 2d day after it.

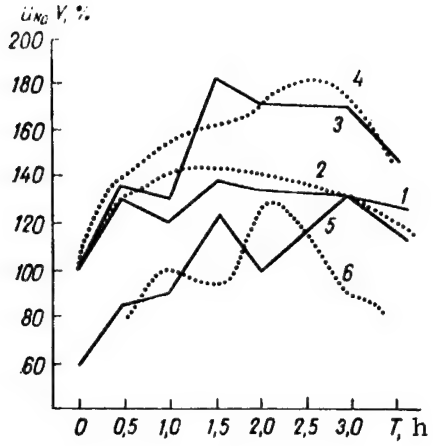


Figure 2.
Model of dynamics of sodium excretion during and after hypokinesia
1, 2) baseline
3, 4) 2d day of hypokinesia
5, 6) 2d day after hypokinesia
Boldface lines--experiment, dotted lines--model

The model's capacity to simualte well reactions of the system of fluid-electrolyte metabolism to certain functional tests confirmed the potential of the chosen direction of research and made it possible to turn to development of more complicated sets of models intended for simulation of elements in the body under extreme conditions. We refer, in particular, to development of a model of body fluid homeostasis, which was worked on jointly with CSSR specialists. The schematic diagram of the model is illustrated here.

A distinction of the new model versions is that there is more detailed analysis of real biomechanical characteristics of the venous compartment of the circulatory system where most blood is deposited, as well as the interstitial environment. The need for consideration of this specific factor had been mentioned rather long ago [12]. Investigations, in the course of which modern methods and equipment were used to measure many parameters characterizing processes of fluid transfer between intravascular and interstitial media, served as a new impetus for development of this direction of modeling.

As shown by calculations with the models, consideration of rigidity and elasticity properties of vascular walls and distinctions referable to flow of osmotic fluids makes it possible to define appreciably the dynamics of the reaction of fluid-electrolyte metabolism to functional loads and to render more logical and natural the process of model identification according to results of real experiments [10].

Further work in this direction is developing, on the one hand, toward integration of existing models with those of other physiological systems, which would permit future simulation of the reaction of the whole body to a set of exogenous factors that determine an extreme situation. Another promising direction is individualization of the model, which takes into consideration the typical values of structural parameters and types of regulation for a given subject or group of subjects. The model's stimulating role in formulating new physiological problems is one of the positive aspects of working on it.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 629.78:613.62

PRELIMINARY RESULTS OF MEDICAL INVESTIGATIONS DURING 5-MONTH SPACEFLIGHT ABOARD SALYUT-7--SOYUZ-T ORBITAL COMPLEX

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by Ye. I. Vorobyev, O. G. Gazenko, Ye. B. Shulzhenko, A. I. Grigoryev, A. S. Barer, A. D. Yegorov and I. A. Skiba]

[English abstract from source] The medical examinations carried out in the 150-day flight were a continuation of the previous studies in terms of the approaches and methods used. The novel approach was a biochemical study of body fluids collected during flight. An important place was occupied by medical monitoring and support performed during EVA. The medical results of the 150-day flight were in consistency with the data obtained during previous spaceflights of similar duration. The health condition and work capacity of the crewmembers throughout the flight (including two EVA events) were good. The changes seen during and after flight were adaptive and disappeared after a relatively short readaptation period.

[Text] A space mission was effected in the Soviet Union, in the period from 27 June to 23 November 1983, aboard the Salyut-7--Soyuz-T orbital complex, manned by V. A. Lyakhov, commander (CDR) and A. P. Aleksandrov, flight engineer (FLE).

Medical inflight tasks were: to conduct an extensive set of medical, sanitary-hygienic and radiobiological studies; further accumulation of data on biological changes occurring during long-term weightlessness; medical monitoring and preventive measures aimed at maintaining a good health status and adequate work capacity during the mission; medical monitoring of cosmonauts during EVA and regulation of this activity as related to their physiological reactions.

The program of medical investigations conducted during and after the mission yielded a large volume of scientific information.

General Description of Flight Conditions

Microclimate parameters were always close to those of earth's atmosphere throughout the mission. It is only on some days, when such operations as extravehicular activity were performed that there were some fluctuations of microclimate parameters.

The overall dose of radiation to which the crew was exposed constituted 1755 mrad, which is considerably less than the permissible levels.

Sanitary and microbiological examination of automicroflora of crew members and microflora of their habitat failed to reveal any new patterns of formation of microflora during the flight. The measures implemented aboard the orbital station effectively maintained the base state of microflora of the crew's integument. At the same time, it was found that the spectrum of antibiotic resistance widened, due to appearance of resistance to ceporin, in some strains of Staphylococcus that are part of the biocenosis of the nasal cavity in one of the cosmonauts. Such changes had also been reported previously in the course of long-term missions.

Analysis of the results of testing microbial contamination of the air environment revealed a tendency, toward the end of the mission, toward increase in total amount of microorganisms, which were represented mainly by commensals of human integument.

As in the case of the preceding long-term mission aboard the Salyut-7--Soyuz-T orbital complex, the diet consisted of a 6-day menu based on using the gourmet-buffet [?] system of stowing food allowances. The food allowance was balanced in all essential ingredients. Mean daily caloric value of the food allowance constituted about 3100 kcal, and actual intake was in the range of 2530-3100 kcal/day.

Water intake was not specially regulated, and it was ad lib. The cosmonauts preferred hot water, using it to prepare tea, coffee, fruit juices and dehydrated main courses. Mean daily intake of hot fluid constituted 1.7 ℓ/person and cold water, 0.12 ℓ. Thus, ad lib intake of fluid constituted an average of about 1.8 ℓ/day/person and, with consideration of liquid content of food allowance (0.5 ℓ) and metabolic fluid (0.4 ℓ), about 2.7 ℓ/day/person, which virtually corresponds to the recommended standard for fluid intake.

The system of preventive measures included daily exercise and wearing G suits, at the final stage of the mission conditioning with lower body negative pressure (LBNP) and intake of fluid and salt supplements at the descent stage and in the immediate postflight period use of special preventive suits.

Inflight Investigations

General Description of Crew's Condition

According to the cosmonauts' self-evaluation, their well-being was good throughout the mission. In the 1st week of the flight both cosmonauts

had the sensation of blood rushing to the head, but it virtually disappeared by the 9th day.

The cosmonauts' appetite was good throughout the mission, sleep was deep and uninterrupted, lasting 6-8 h.

The crew's work capacity was rather high. By the end of the work day, both cosmonauts reported fatigue, which disappeared after a night's sleep.

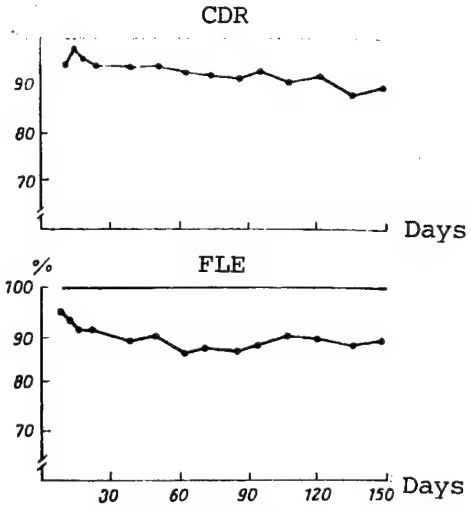

Figure 1.
Dynamics of leg volume in crew during 150-day mission aboard Salyut-7--Soyuz-T orbital complex

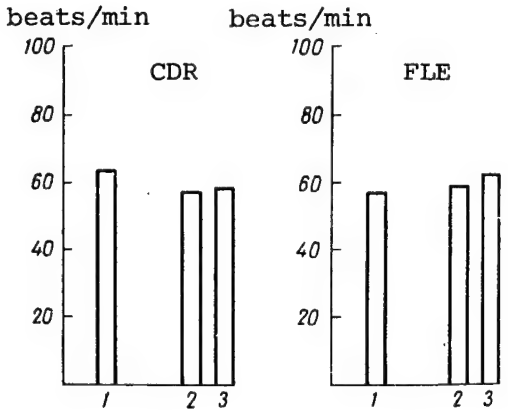

Figure 2.
Changes in mean HR at rest during and after 150-day mission
Here and in Figure 3:
1,2,3) mean values, preflight, in 1st and 2d-5th flight months, respectively

Anthropometric tests revealed a decrease in body weight and leg volume. Maximum decrease in leg volume constituted 9.9% for the CDR and 13.7% for the FLE (Figure 1).

Heart rate (HR) at rest was in the range of 48-72/min in the CDR (52-71/min preflight) and 58-70/min in the FLE (52-60/min preflight) (Figure 2).

Arterial pressure (BP) of the CDR was characterized by a tendency toward decline of diastolic and lateral systolic pressure in the absence of appreciable changes in end systolic and mean pressure. In the FLE, mean BP rose somewhat in the 1st month of the mission, then had a tendency toward normalization in the 2d-5th months.

As a result of testing bioelectric activity of the myocardium (9 conventional leads), CDR presented a decrease in amplitude of $R_{i,V_{2-6}}$ and $T_{V_{I},V_{3-6}}$ waves;

the FLE presented a decrease in amplitude of R_{I,III,V_{1-4},V_6} and T waves in

the standard and right thoracic leads. Analogous wave changes, with retention of shape and position of ST segment, had been also observed in other long-term missions, including the CDR during a 175-day flight. They could have been attributable to positional changes or else they reflected distinctions of myocardial metabolism during long-term weightlessness.

Investigations During LBNP Test

HR (Figure 3) during the LBNP test generally corresponded to preflight values in the CDR (preflight 60-76/min, inflight 63-70), whereas the FLE presented a tendency toward rise of this parameter (preflight 66-71, inflight 70-79) in the 2d-5th month.

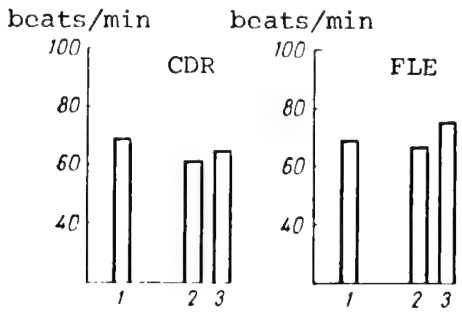

Figure 3.
Changes in mean HR during test with LBNP (-35 mm Hg) before and during 150-day mission

BP parameters during LBNP virtually corresponded to preflight values in the CDR, whereas in the FLE they were lower, on the average in the 2d-5th month than preflight.

Rheographic examination revealed a decrease in pulsed filling of cerebral vessels in the CDR. In the FLE, the hypotensive base state of cerebral vessels, which persisted throughout the mission, became normotensive during LBNP and came close to preflight values.

Investigations During Test With Graded Physical Exercise

During the graded physical load (GPL), HR of CDR increased to about the same extent in most cases as preflight (preflight 121-129/min, inflight 117-131). In the FLE, this parameter rose to 117-134/min during the inflight test (112-123 preflight). The HR/force ratio fluctuated within the range of preflight values in all cases. Time of establishment of stable state and rate of restoration of HR corresponded to preflight data.

Circulation volume (CV) during GPL increased within the range of preflight values in the CDR and somewhat less in the FLE.

The BP changes in the 1st min after GPL were characterized in the CDR for the first 3 months of the mission by greater elevation of the systolic components than before the flight. In the FLE, in about the same period, the dynamics of several parameters presented signs of development of a stepped type of reaction, where greater increment of diastolic and end systolic BP was observed in the 2d min than in the 1st, and there was also greater increase in stroke volume.

In view of the above-described reactions, tolerance to tests with GPL was assessed as satisfactory in the CDR in the 1st-3d months and in the FLE in the 1st-2d months of the mission. During the rest of the flight, both crew members were evaluated as having good tolerance to functional tests.

Physiological and Hygienic Aspects of Extravehicular Activity

During the two space walks (lasting 170 and 175 min) by the crew on the 128th and 130th days of the mission (1 and 3 November 1983), they installed additional solar batteries. The duration of work (total of 5 h and 45 min) was not limited for physiological and medical indications. They wore a semirigid space suit for EVA, which had a self-contained life-support system and was designed for continuous use for 5 h. A liquid-cooled garment was used to maintain the temperature balance of the body, with manual control of water temperature in accordance with heat perception. Prebreathing during decompression and maintaining a rather high absolute pressure (280-300 mm Hg) in the space suit prevented caisson disease. An atmosphere was produced that was close to one of pure oxygen, with partial CO_2 pressure of less than 10 mm Hg.

During both EVA's, the cosmonauts felt well and reported fatigue due to work after the operations.

Results of medical monitoring during decompression and EVA activity

Date	Day of flight	Activity	Crew member	HR/min	RR/min	Expended energy, kcal/min
01.11.83	128	Work in spacesuit in station (decompression)	CDR	106—132	10—20	3,0
			FLE	75—116	16—24	2,6
			CDR	81—119	36—48	3,8
		Work in spacesuit during EVA	FLE	78—117	24—36	4,9
03.11.83	130	Work in spacesuit in station (decompression)	CDR	91—132	12—20	3,1
			FLE	67—114	16—24	2,6
		Work in spacesuit during EVA	CDR	74—108	16—40	3,3
			FLE	66—107	24—36	4,3

During EVA there was a rise in HR (maximum 119/min in the CDR and 117 in the FLE) consistent with work load. Respiration rate (RR) increased noticeably (maximum 48/min for the CDR and 36 for the FLE). During performance of the second operation, maximum changes in some physiological parameters (HR and energy expenditures of both cosmonauts, RR in the CDR) were somewhat less marked than during the first (see Table).

Mean energy expenditure during EVA constituted 3.8 kcal/min in the CDR and 4.9 kcal/min in the FLE during the first EVA and 3.3 and 4.3 kcal/min, respectively, during the second. Minimum energy expenditure and heat removal of 2-3 kcal/min were referable to the rest period in the "shade." Maximum energy expenditure and heat removal (6-7 kcal/min) were observed during performance of final operations to open the solar battery (when FLE operated the crane), as well as when closing the exit hatch (about 5 kcal/min in the CDR). Overall energy expenditure and heat removal for the entire period (about 4.5 h) in the space suit constituted about 1000 kcal for the first exit and about 800-900 kcal for the second. During the 170 and 175 min of EVA, total O_2 uptake ranged from 107 to 127 ℓ (STPD), constituting a mean of 0.7 ℓ/min.

Upon completion of EVA, there was no marked fatigue and, according to the cosmonauts' reports, the operation was easier than during training on the ground.

In spite of the full program of different operations during EVA, the quality of heat regulation was satisfactory and body temperature did not exceed the permissible range. Body temperature in the mastoid region after putting on the space suit varied in the "comfort" range of 35.2 to 36.8°C in the CDR and 34.6 to 36.4°C in the FLE.

These findings enable us to conclude that there was rather effective organization of the cosmonauts' work outside the orbital station. Reliable operation of systems, sufficient flexibility of the space suit and purposeful physical conditioning of the cosmonauts (both before and during flight) provided for complete fulfillment of EVA program with good physical condition and well-being of cosmonauts.

Biochemical Tests

Biochemical analysis of urine was performed using the Plasma-01 set of instruments developed and manufactured in CSSR, in order to determine the state of fluid-electrolyte metabolism in flight. This set is designed to collect, store and transport specimens of biological material taken during spaceflights. When delivered to earth, the specimens were analyzed under laboratory conditions.

One of the crew members collected urine for 3 days twice during the mission: on the 43d-45th and 86th-88th days. Samples were taken of the collected urine, which were frozen and delivered to earth for analysis. In these samples, sodium, potassium, magnesium, chlorine, phosphorus, osmotically active substances, creatinine, urea, a number of hormones and biologically active substances were assayed.

The results of these analyses (A. S. Ushakov, V. B. Noskov, I. A. Popova et al.) revealed that there was a decrease in inflight concentrations of most electrolytes, as well as creatinine and urea. At the same time, there was a decrease in concentration of antidiuretic hormone in urine (Footnote 1)(For technical reasons, diuresis was not measured).

In addition to change in concentrations of electrolytes, there was a change in their proportion in urine during the mission. Thus, the sodium/potassium ratio, which is an indirect indicator of mineralocorticoid activity, rose on the 43d-45th days of the mission and dropped on the 86th-88th days, mainly due to decrease in urine sodium concentration. Calcium/magnesium and sodium/potassium ratios also decreased. Inflight total levels of osmotically active substances in urine were lower than preflight. Perhaps, the low level of intake of table salt on the days of collecting urine during the flight was one of the causes of reduced sodium concentration. On these days, ad lib fluid intake constituted about 1700 mℓ/day and total fluid intake was somewhat more than 2 ℓ, which conformed to the usual fluid intake on the ground.

Determination of parameters characterizing metabolism of steroid hormones revealed that, on the 43d-45th days of the spaceflight, the concentration of

aldosterone and cortisol in urine decreased with concurrent relative increase in the fraction of bound cortisol, which is indicative of a change in steroidogenesis.

By the 88th day of the mission, urine concentration of aldosterone, cortisol and testosterone increased both in the daytime and at night. The change in steroid metabolism, which was observed only with respect to glucocorticoids in the first test, began to be observed also with reference to mineralocorticoids.

In the postflight period, there was an increase in excretion in urine of steroid hormones--cortisol, testosterone, aldosterone, as well as antidiuretic hormone. However, excretion of osmotically active substances, including sodium, decreased and, at the same time, there was increase in osmolality and concentration of blood serum sodium and calcium. These data are indicative of toning of hormone systems to retain fluid and electrolytes in the body in the early postflight period in order to maintain adequate fluid-electrolyte homeostasis.

Thus, the results of the "Metabolism" experiment showed, for the first time, that changes in steroidogenesis and corticosteroid metabolism, which had been repeatedly demonstrated after spaceflights, arise and develop during weightlessness. They are attributable, in part, to changes in fluid-electrolyte metabolism and, at later stages of the mission, they are aimed at maintaining ion homeostasis.

The distinctions of inflight carbohydrate metabolism were investigated by Soviet and French specialists by means of studying the glycemic curve after intake of carbohydrates (K. V. Smirnov, L. G. Ruvinova et al.). For this purpose, fasting blood glucose, then glucose content every 30 min after a carbohydrate load (28 g sugar + 28 g glucose) for 90-120 min were measured in one of the cosmonauts before the mission and on the 60th and 88th days of the flight using a glucosometer.

Fasting blood sugar and postload glucose level dropped on the 60th day of the flight, as compared to the preflight period. There was some slowing in utilization of glucose. On the 88th flight day, glucose content of fasting blood and after the load increased somewhat. However, unlike the preflight and 60th day data, there was slower utilization of glucose.

On the 25th postflight day, the glycemic curve was similar to the one for the 88th flight day. On the 55th day of the recovery period, there was restoration of glucose homeostasis, according to analysis of the glycemic curve.

Analysis of the obtained data indicates that the observed changes in the glycemic curve on the 60th flight day probably reflect depression of processes of hydrolysis and transport of carbohydrates in the gastrointestinal tract, with their stabilization by the 88th flight day. Evidently, in this case, there are also functional changes in the insular system of the pancreas, as manifested by delayed utilization of glucose.

Results of Postflight Studies

The cosmonauts' well-being was relatively good at the landing site. In supine position, they presented no complaints, whereas when they attempted to assume an erect position they experienced mild vertigo. They also reported fatigue.

Medical examination at the landing site showed 82-110/min HR in the CDR and 72-102/min in the FLE. BP constituted 110/80 and 115/70 mm Hg, respectively.

The cosmonauts' assessed their well-being as good 7-8 h after landing. Examination revealed vesicular respiration, heart sounds were rhythmic, dull, without murmurs. In both cosmonauts, HR was 72/min and BP constituted 120/90 and 120/80 mm Hg. In seated and standing positions, vertigo, sensation of discomfort and nausea were reported by one of the cosmonauts. All these signs disappeared rapidly when he changed to horizontal position. Both crew members presented signs of asthenization in the form of rapid fatigability with diverse loads, diminished work capacity and emotional lability.

Body weight dropped after landing, as compared to preflight value: by 3.5 kg in the CDR and 5.7 kg in the FLE. This parameter was restored on the 8th-9th day in both cosmonauts.

Examination of vestibular function (L. N. Kornilova, I. K. Tarasov et al.) revealed that both cosmonauts presented impaired statokinetics after the mission, in the form of change in gait and instability in Romberg's position. Head movements elicited vertigo and discomfort. This was associated with stable, rhythmic, continuous nystagmus.

Examination of otolith function revealed hyperreflexia and asymmetry of reactions. The latter phenomenon, along with rise of thresholds, was also observed in the examination of reactivity of the system of semicircular canals. Spatial orientation in relation to the gravity vertical was associated with increased error in perception of spatial coordinates and appearance of error asymmetry in lateral positions. The signs of vestibular dysfunction persisted for 7 days in the CDR and 3 days in the FLE.

Examination of motor functions (I. B. Kozlovskaya, Yu. V. Kreydich et al.) revealed moderate decline in strength of anterior and posterior crural muscles (according to isokinetic and isometric dynamometry). In assessing sensory inputs (static and muscular), some decline was demonstrated in thresholds of vibration sensitivity of supporting zones of the foot in the CDR and alleviation of thresholds of muscular reception in both cosmonauts. There was also a change in control of erect position, which was manifested by increase in amplitude of fluctuation of general center of gravity, presence of marked high-frequency oscillations of the tremor type, longer time of recovery of body equilibrium after use of graded perturbations.

The motor system changes diminished or disappeared entirely by the 11th postflight day. According to the foregoing, the changes were the most marked in the system of movement coordination and, to a lesser extent, in the muscular system; they were minimal in the reflex and afferent systems. The

persistent decline of strength characteristics of crural muscles, which was also observed on the 11th postflight day, could be related to the assumed development of subatrophic or atrophic processes in muscles due to inadequate load.

Examination of the cardiovascular system (A. F. Zhernavkov et al.) revealed that resting HR was elevated. There were electrocardiographic signs of metabolic changes in the myocardium (diminished amplitude of T wave in all leads), some decline of end systolic and diastolic heart volume (by 10-15%), orthostatic and physical deconditioning.

Biochemical blood tests (I. A. Popova et al.) revealed that, on the 1st postflight day, both cosmonauts presented a lower level of tissue metabolism, as manifested by decrease in basic substrates of intermediate products of carbohydrate metabolism (lactic and pyruvic acids) and blood serum enzyme activity, in particular that of malate dehydrogenase.

By the 8th day of the recovery period, there was restoration of intensity of metabolic processes to the preflight level according to most tested parameters. At the same time, there was appreciable increase in overall activity of blood creatine kinase with concurrent activation of both myocardial and muscular isozyme in one of the crew members and of alanine transaminase in the other. Hyperenzymemia to varying degrees had been observed repeatedly before following long-term spaceflights, as well as after long-term bedrest. Both activation of tissue metabolism and changes in membrane permeability of cellular structures could be the probable causes of increase in blood enzyme activity in the recovery period. By the 60th day of the recovery period there was restoration of enzymemia level.

Hematological tests (V. I. Legenkov et al.) established that, on the 1st postflight day, there was a decrease in erythrocyte, hemoglobin content of blood and decline of hematocrit. The Price-Jones curve was indicative of microcytosis in blood. At later stages, there was a reticulocyte reaction reflecting erythropoietic activity.

Investigation of parameters of energy metabolism of erythrocytes (A. S. Ushakov et al.) (levels of adenosine triphosphatase--ATP, 2,3-diphosphoglycerate--2,3-DPG, reduced glutathione--GSH, activity of lactate dehydrogenase--LDH and glucose-6-phosphate dehydrogenase--G-6-PD) revealed the same changes as following other long-term flights: decrease in ATP, insignificant decrease in GSH, as well as increase in activity of LDH, G-6-PD and in amount of 2,3-DPG in erythrocytes, as compared to preflight values.

Investigation of digestive system function (K. V. Smirnov et al.) before and after the flight was conducted on the basis of determination of enzyme-secreting function of the stomach, pancreas and small intestine. On the 1st postflight day there were no deviations whatsoever in activity of gastric and pancreatic enzymes in blood. For the first 5 days of the postflight period, there was a tendency toward increase in urine lipase activity in both cosmonauts, which is indicative of some functional changes in the exocrine part of the pancreas.

By the 7th day of the recovery period there was some increase in activity of pancreatic amylase in blood, which was twice as marked in the FLE, and rise in level of invertase and maltase (enzymes that split disaccharides in the small intestine) in feces.

The findings are indicative of changes inherent in the change from weightlessness to normal activity at earth's gravity and they are related primarily to the need to provide the body with an energy substrate--glucose. However, according to the results of analysis of the glycemic curve in response to a carbohydrate load, it can be assumed that energy is supplied to the body in weightlessness to a greater extent by another substrate--fatty acids.

Immunological studies (I. V. Konstantinova et al.) revealed that there was postflight decrease in activity of normal killers in both cosmonauts (by a mean of 60%), as well as in functional activity of T lymphocytes, this being associated with concurrent decrease in blood T lymphocyte content in the FLE. In the CDR, there was sensitization to Proteus and in the FLE, some increase in IgM in blood serum. All this is indicative of development of certain inflight changes in the cosmonauts' immunity system, the most significant of which is some decline in resistance to viruses and function of T lymphocytes, which is consistent with results obtained from previous long-term missions.

Thus, the studies conducted during and after the 5-month flight failed to demonstrate qualitatively new changes in health status of the cosmonauts. Use of a set of preventive measures provided for a good physical condition and adequate work capacity throughout the mission (including installation work outside the station). The observed changes in different systems of the body were adaptive, they conformed to prevailing factors, they did not affect work capacity and fulfillment of flight program, and they disappeared entirely in the recovery period.

The extensive studies conducted inflight, which included several biochemical tests performed for the first time, yielded additional information about changes in a number of functions in weightlessness, including the effect of long-term flight on fluid-electrolyte homeostasis. In particular, it was demonstrated that, under flight conditions, there is formation of a different hormonal background, as compared to the one on the ground, while the set of factors present during landing and with earth's gravity at the early postflight stages enhances these changes.

Thus, the obtained data confirmed once more the possibility of efficient and multifaceted performance by man under the conditions of a long-term spaceflight.

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PROFESSIONAL WORK CAPACITY AND FUNCTIONAL STATE OF OPERATOR EXPOSED TO REPEATED OPTOKINETIC AND ANTIORTHOSTATIC FACTORS

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[Article by L. N. Kornilova, L. D. Smirichevskiy, A. V. Trutnev, S. L. Chekanova, I. Ya. Yakovleva and S. L. Kravchenko]

[English abstract from source] It has been shown that optokinetic stimulation that elicits sensory-autonomic manifestations of motion sickness and head-down tilt that simulates fluid redistribution in the cranial direction decrease professional abilities of the operator even after he has developed good skills. Repeated exposures to optokinetic stimulation or head-down tilt have some training effect. However, control tests that include both optokinetic stimulation and head-down tilt give evidence that their training effect is not adequate.

[Text] At the early stages of adaptation to weightlessness, among the functional disorders a significant place is referable to the symptoms of motion sickness, which is usually related to impaired functional coordination of analyzers ("sensory conflict") and shifts of blood and spinal fluid in a cranial direction [5, 6, 9-12]. In this regard, it is deemed desirable to investigate the role of different etiological factors in development of vestibulovegetative and spatial disorders during simulation of some of the effects of weightlessness, as well as the influence of sensory and autonomic manifestations of motion sickness on operator performance.

Our objective here was to investigate professional work capacity and the functional state of an operator exposed repeatedly to optokinetic and antiorthostatic [head-down tilt--HDT] factors.

Methods

The studies were conducted using a simulator situated in a small chamber (6 m^3). The subject was immobilized in a reclining chair. The factors we used were optokinetic stimulation (OKS), which elicited development of motion sickness symptoms [7, 8], and redistribution of body fluids to the upper half of the body, which was induced by dropping the head end of the recliner to -30° angle for 1.5 h [1, 3].

We examined a set of physiological reactions: pulse rate (PR) from the electrocardiogram (ECG), arterial pressure (BP), degree of blood filling of the head using the rheoencephalogram, parameters of cardiointervalography with calculation of tension index (TI), mode, amplitude of mode and range of variation. We determined the intensity of autonomic reactions (AR) according to Khilov, frequency and velocity of slow phase of optokinetic nystagmus (OKN) in the 1st min of OKS, accuracy of perception of spatial coordinates. We also determined accuracy of perception of the vertical in the presence of optokinetic interference, as well as quality of operator work--precision and time of optical manual orientation for heading, bank and pitch.

The 1st series of studies consisted of training only on the program of operator work. There was preliminary training (2-3 times), then 16 exercises at the rate of 2 per day or every 1-2 days (breaks for days off) until stable skills were acquired.

The 2d series involved working under analogous conditions but in the presence of OKS, which elicited the symptoms of motion sickness. OKS [8] was used for 10 min before working on the operator program and for 20 min during work.

In the 3d series, the subjects performed operator work in antiorthostatic position (at an angle of -30° for 1.5 h).

Control tests were used to evaluate the efficacy of the training cycles: after the 1st series--operator work when a stable skill was developed against the background of 30-min OKS; after the 2d and 3d series--the same in antiorthostatic position.

All of the series of studies involved the same 16 healthy men 25-45 years of age. There were intervals of 2-2.5 months or more between series. Before each series, we checked retention of operator skill and determined the level of vestibular (vestibulovegetative) [4] and optokinetic [7] stability.

Upon completion of all series, we determined the parameters of optokinetic and vestibular stability. Duration of retention of training effect was checked by the results of repeating the control test after 1 month.

Results and Discussion

The baseline examination enabled us to single out individuals resistant to vestibular (4 men) and optokinetic (8 men) stimulation (10 min with 0 AR [autonomic reaction]), as well as those who were not resistant to both types of stimulation (4 men). Tolerance to the test of I. I. Bryanov [4] lasted 1 to 6 min in the nonresistant subjects, with grade I-II or II autonomic reactions, tolerance to OKS lasted 8-10 min, but with grade I-II AR.

It must be noted that of the four subjects with vestibular resistance, one presented diminished resistance to OKS, and of the eight resistant to OKS two presented a low level of vestibular resistance.

As a result of the first training series, a skill was developed in performing regular work, there was an increase in accuracy of operations, decrease in time spent to perform them, decrease in fluctuations of PR and BP; TI fluctuations were in the range of a physiological reaction.

After development of a stable skill, the subjects were asked to take a control test--regular operator work in the presence of graded optokinetic stimulation (30 min).

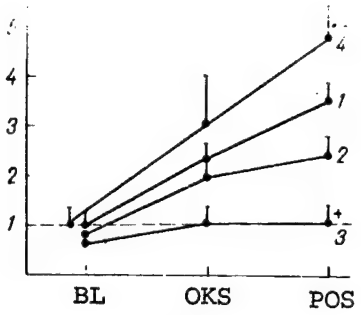

Figure 1.
Parameters of manual orientation (course in degrees) in subjects with different levels of optokinetic and vestibular resistance in presence of optokinetic disturbances

Here and in Figure 3, horizontal dash line indicates normal values.

Here and in Figures 2-4:

1) subjects with vestibular resistance
2) " without " "
3) " with optokinetic resistance
4) " without " "

POS) after exposure to OKS

BL) baseline--here and in Fig. 2, 3, 4

Mean values and standard deviations given

Asterisk (Figures 1-4) indicates reliable differences from baseline ($P<0.05$) and + shows reliable intergroup differences ($P<0.05$)

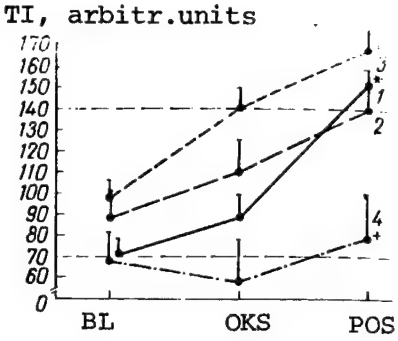

Figure 2.
Dynamics of tension index during manual orientation with OKS in subjects with different levels of optokinetic and vestibular resistance

Here and in Figure 4 the horizontal dash lines show range of TI changes under normal conditions

Analysis revealed that OKS worsens professional performance (Figure 1). In subjects without optokinetic resistance there was statistically reliable increase in error when performing operator work. The work was performed with marked autonomic reactions (AR-I and AR-I-II), with 10-12/min increase in PR and change in dynamics of TI. In subjects with vestibular and optokinetic resistance (Figure 2), there was an adequate reaction in the form of increase in TI from 96 to 142 units (mean data), whereas in those without OKS resistance there was an inadequate reaction--TI decline to below normal during exposure, which could be a reflection of stress of regulatory mechanisms [2]. Two out of the 16 operators were unable to perform the program of operator work.

The results of the 2d series of studies revealed that repeated use of OKS during performance of operator work has some conditioning influence (Figures 3a and 4a). Upon completion of the training cycle, OKS was not associated with

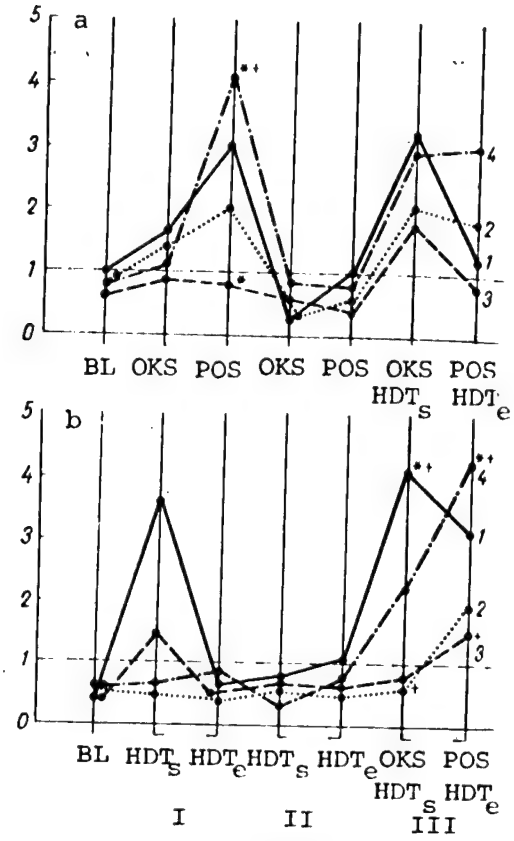

Figure 3.
Dynamics of bank (degrees) during manual orientation when conditioning for OKS S (a) and for HDT (b)

Here and in Figure 4:
HDT$_s$, HDT$_e$) start and end of head-down tilt
I) first training
II) sixth
III) control test

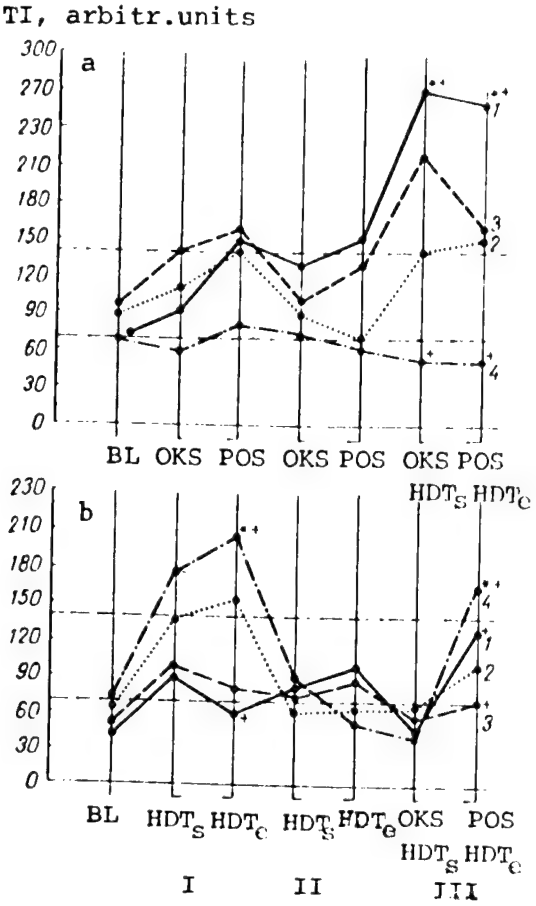

Figure 4.
Dynamics of tension index of cardiac function during manual orientation of "object" during conditioning for OKS (a) and HDT (b)

development of motion sickness symptoms, and elements of operator work were performed rather accurately and within a short time. After conditioning for OKS we were able to observe restoration of skill in operator work that had been lost as a result of the first exposure to OKS. However, there was persistence of some differences in reactions, depending on base resistance to OKS. Thus, resistant subjects retained an adequate TI reaction to OKS (moderate increase slightly above the physiological fluctuations at rest) (see Figure 4a), whereas nonresistant subjects also presented an adequate reaction but with wider fluctuations of TI. In the control test (combination of OKS and redistribution of blood), reliable increase in TI (to 267 units) was observed in subjects with vestibular resistance. Those with high sensitivity to OKS reacted differently: exposure was associated with decline of TI from 66 to 48 units (according to mean data). There was poorer accuracy of perception of vertical line and greater fluctuations of BP and PR. Some subjects again developed signs of autonomic discomfort and poorer parameters of operator performance; four men were entirely unable to cope with the program of operator work.

The training cycle with redistribution of blood to the upper half of the body (3d series) helped attenuate autonomic reactions to this factor. Performance of operator work with HDT improved distinctly by the 5th-6th training session (Figure 3b) and there was less fluctuation of TI (Figure 4b). According to the results of rheoencephalography, there was substantial decrease in pulsed flow of blood to cerebral vessels due to increase in arterial and venous vascular tonus. There was decrease in total delivery of blood to the head due to improved venous efflux, i.e., physiological reactions were formed that prevented excessive displacement of blood and body fluids to the upper half of the body in HTD position. However, performance of the control test after the training cycle, with combined exposure to redistribution of blood and OKS, was indicative of an insufficient conditioning effect of the training series used with separate exposure to one of the simulated flight factors. As can be seen in Figures 3b and 4b, OKS again worsened operator performance and parameters of physiological reactions.

After completion of all series of training there was insignificant increase in duration of tolerance to vestibular factors, less marked AR in subjects with low vestibular and optokinetic resistance.

To sum up the results of the three series of studies, it can be noted that successive implementation of separate training cycles for operator work, exposure to OKS with development of the symptoms of motion sickness, head-down tilt, which elicits redistribution of blood to the upper half of the body, does not provide for stable retention of skill in operator work in the case of combined exposure to the factors listed.

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VENOUS PRESSURE IN JUGULAR VEIN SYSTEM AND EFFECTIVENESS OF BLOOD RETURN TO RIGHT HEART DURING 120-DAY HEAD-DOWN TILT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by V. G. Doroshev]

[English abstract from source] Study of time-course variations of venous pressure in the jugular veins can be used to identify individual adaptation to prolonged head-down tilt. The method of measuring blood return to the right heart presented here can be employed to evaluate the efficacy of countermeasures during head-down tilt and to predict orthostatic tolerance after it.

[Text] Investigation of the human circulatory system during long-term spaceflights and under simulated conditions revealed signs of redistribution of blood in a cranial direction and relative deconditioning of the cardiovascular system, manifested primarily by diminished orthostatic tolerance [1, 4, 6, 7]. Prompt detection and prediction of adverse states due to exposure to spaceflight factors are important to determination of efficacy of preventive measures, as well as for prompt correction of work and rest schedule of crew members in order to improve their work capacity [2, 5].

Investigation of dynamics of venous pressure in jugular veins and effectiveness of blood return to the right heart during 120-day antiorthostatic hypokinesia [HDT--head-down tilt] are the logical continuation of accumulation of scientific data in order to solve the problems under study.

Methods

The investigations were conducted with the participation of 14 healthy men 25 to 41 years of age (mean age 33.4 years). For 120 days, the subjects were submitted to HDT with the head end of the bed tilted down at an angle of -4°. Throughout the study period, they were on the same diet and fluid intake regimen. The subjects were divided into four groups. The first served as a control, the 2d performed special exercise on a program developed by I. B. Kozlovskaya and A. V. Ovsyannikov (development of endurance and strength), which was supplemented with passive-active stretching of certain

muscle groups. The 3d group of subjects were given a set of pharmacological agents on a program developed by A. I. Grigoryev, B. V. Marukov and Yu. V. Sukhanov, aimed primarily at antidemineralization of bone and correction of lipid metabolism. For the fourth group, we used a combination of physical training and pharmacological agents as preventive measures.

Examination of venous pressure (VP) in the system of the jugular veins was performed using the method described in [3] with a module of the Polynome-2M equipment. We recorded the venous-arterial pulsogram (VAP) from a projection of the jugular veins at relative rest and in horizontal position. The VAP changes into a sphygmogram (SPG) of the carotid artery when the head end of the bed is smoothly moved to vertical position (at angles of +3 to +15°). At the time when the bed stops moving, determination was made of the angle of rotation. VP was calculated using the formula: $P = 0.735 \cdot l \cdot \sin L$, where 0.735 is the correction factor, l is distance from the right atrium to the parietal region (in cm) and sinL is the angle of rotation in relation to the horizontal plane.

After measuring VP, the subject performed static exercises with both feet, bracing them on special pedals, with tension (pressure) of 110-160 mm Hg. This was associated with reverse transformation of SPG into VAP. At this time, we recorded pressure on the pedals, and the static load was not further increased. With the subject holding the (demonstrated) static pressure for 40-70 s, the head end of the bed was raised to a larger angle until VAP changed to SPG and, using the above formula, we again calculated the angle of elevation and VP. Maximum elevation of the head end of the bed when measuring VP did not exceed 15° from the horizontal plane.

The coefficient of effectiveness of blood return (CEBR) to the right heart was calculated using the formula:

$$CEBR = \frac{\Delta VP}{SL} \cdot 100$$

where ΔVP is the difference in VP with static load and base VP, SL is static load (in mm Hg).

VP was measured in the morning, 1-1.5 h after breakfast in the baseline period and on the 2d, 5th, 49th, 70th, 90th and 119th days of HDT.

Results and Discussion

The subjects were arbitrarily divided (Table 1) into those with lose baseline pressure (mean of 2.37 mm Hg with range from 1.54 to 3.59 mm Hg) and normal pressure (mean 4.68 mm Hg, variability from 4.6 to 6.62 mm Hg) in accordance with VP level before the study.

During HDT, VP dynamics were individual and presented the following tendencies: it became lower than baseline values and, in some cases, was not demonstrable at all; VP dropped relatively with periodic return to baseline levels and subsequent progressive elevation; VP rose significantly with period drop to baseline levels. On the 119th day of HDT, 1 subject with low pressure showed 42%

elevation, in 3 cases it remained at the baseline level and in 7, it dropped by a mean of 43.5% (ranging from 20 to 100%), as compared to baseline values. In 3 subjects with normal VP in the baseline period, it dropped by a mean of 31% on the 119th day. However, its absolute values exceeded those recorded in subjects with low VP in the baseline period.

Table 1. Dynamics of VP (mm Hg) in system of jugular veins during HDT

Subject	Conditions	Baseline	Day of HDT					
			2	5	49	70	90	119
B-ev	C	2,56	0	0,51	0	0	2,05	2,05
G-yuk	C	6,11	3,59	4,60	3,59	6,11	5,61	3,59
L-ev	C	1,54	1,03	0	0	2,56	1,54	1,54
G-in	PT	2,56	0,51	0	1,28	3,06	2,56	1,54
Z-ov	PT	2,05	0	0	4,09	0	0	2,05
B-ov	PT	2,31	0,51	2,31	1,28	1,09	2,05	0
G-ov	PA	3,33	2,56	2,05	0	2,05	2,05	2,05
K-in	PA	3,59	3,59	2,56	0	4,09	3,06	2,05
Zh-ov	PA	3,56	2,31	3,06	0	0	4,09	2,05
K-in	PA	6,62	6,62	7,61	—	7,11	5,10	4,09
Ch-ov	PT+PA	2,05	0	1,03	2,89	0	2,05	2,05
S-ov	PT+PA	2,56	5,10	2,05	1,03	7,61	5,10	2,05
V-ov	PT+PA	4,60	0	1,79	4,60	4,09	1,53	4,09
Kh-in	PT+PA	4,59	2,05	1,28	2,56	4,09	3,06	5,10

Key, here and for Table 2:

C) control
PT) physical training
PA) pharmacological agents

Table 2. Dynamics of CEBR of blood return with static load during HDT in relation to baseline VP

Subjects	Conditions	Base line	Day of HDT						Prediction of OT	Actual tolerto POT
			2	5	49	70	90	119		
B-ev	C	0	0	1,28	0	0	0	0	U	U
G-yuk	C	1,0	0,8	2,33	1,68	1,36	0,9	1,25	G	U
L-ev	C	0,95	2,13	0	0	0	0	0	U	U
G-in	PT	0,85	1,85	2,72	3,78	2,90	3,84	0,92	U	U
Z-ov	PT	0	0	0	0,77	0	0	0	U	U
B-ov	PT	0	0	0,85	0	0,64	0	0	U	U
G-ov	PA	0,50	1,17	0,84	2,13	2,77	1,85	1,28	G	S
K-in	PA	1,16	0,80	1,70	1,86	1,68	1,85	1,82	G	G
Zh-ov	PA	1,61	0,98	0	0	0	2,10	1,85	G	G
K-in	PA	1,58	0	0	4,77	0	1,26	2,40	G	G
Ch-ov	PT+PA	0,84	1,70	0,40	0,85	1,72	1,70	1,40	G	G
S-ov	PT+PA	1,36	0,77	1,67	0,92	0,90	0,84	5,05	G	G
V-ov	PT+PA	0,80	0	1,91	1,34	0,84	1,39	2,10	G	G
Kh-in	PT+PA	2,02	1,49	1,06	0,41	0,84	0,93	2,28	G	G

Key:

OT) orthostatic tolerance
POT) passive orthostatic test
U) unsatisfactory
S) satisfactory
G) good

In the acute period of adaptation to HDT, on the 2d and 5th days of the experiment, VP was virtually undemonstrable or equaled 0 in 7 subjects, dropped by 20-80% in 16, remained at the base level in 3, exceeded the baseline values by 15 and 99% in 2 subjects. In the case of elevated VP, there was increase in amplitude of *a* wave on the VAP; however, the *a/c* amplitude ratio was less than 1. Typically enough, in the case of low VP, as compared to the baseline values, *a/c* ratios were also less than 1. During the periods when VP was not demonstrable, the SPG was recorded, which could be due to the two following causes. First of all, in the acute period of adaptation to HDT there was considerable increase in diuresis, which led to decrease in circulating blood volume and natural decline of central venous pressure. In addition, in the case of significant elevation (by more than 2 times) of VP, there can be overstretching of the walls of the jugular veins and their pulsation may stop. However, these assumptions do not yet have sufficient experimental confirmation.

With increase in duration of HDT, VP remained essentially below baseline levels. Thus, in the group given pharmaceutical agents, no VP was demonstrable on the 49th day. The decline of VP on the 119th day in this group was virtually identical when expressed as percentage and absolute value. It must also be noted that substantial elevation (1.5-2-fold) of VP, as compared to baseline levels, was observed in all groups (with exception of the control group) on the 70th and 90th days of HDT. Such VP changes could be attributable to the direct effect of the preventive agents and, perhaps, were due to fatigue elicited by intensive physical exercise. Ye. M. Yuganov et al. [6] cite data indicative of analogous changes in VP dynamics during spaceflight, and they were usually due to intensification of work aboard the orbital complex [6].

On the 119th day of HDT, VP held at baseline levels in 3 subjects, exceeded them in 1, was below them in 9 and was not demonstrable in 1 subject.

The changes in VP dynamics during HDT were not always associated clearly enough with the subjective state of the subjects. In spite of the appreciable elevation of VP in S-ov, he did not experience the sensation of blood rushing to the head. In B-ov, on the contrary, such a sensation was distinct on the 5th day of the study, although his VP was on the base level on that day. In Z-ov, VP equaled 0 in the acute period of adaptation, whereas on the 49th day of HDT it was double the baseline value. On the 1st day of HDT, this subject presented no complaints, but on the 49th day he was bothered by headache.

These findings stress the individual nature of adaptation to changes in hydrostatic pressure, due probably to distinctions of proprioceptive sensitivity and condition of collaterals.

In the background period, CEBR equaled 0 in 3 subjects, was less than 1 in 5 and more than 1 in 6 cases. On the 2d and 5th days of HDT, CEBR equaled 0 in 9 cases, showed relative decline in 6 and rose in 11 cases (Table 2).

In the course of further HDT, CEBR equaled virtually 0 in 4 subjects.

In Zh-ov, CEBR was 0 on the 5th, 59th and 70th day, but thereafter it exceeded background values. In the other 10 subjects, CEBR showed an overt tendency toward rising in the course of the study.

Evaluation of individual dynamics of CEBR enabled us to establish that during HDT without preventive agents or with use of exercise alone there was no improvement of return of blood to the heart; use of pharmacological agents resulted in a moderate elevation of CEBR. The combination of pharmacological agents and exercise was the most effective means of raising the CEBR during HTD.

A prognostic evaluation was made of orthostatic tolerance (see Table 2) on the basis of CEBR values on the 119th day of HDT, and it was checked against the results (according to the data of V. I. Lobachek) of tolerance to a passive orthostatic test (good, satisfactory, unsatisfactory). In only 2 of our 14 cases the prediction was wrong or partially incorrect.

This warrants the belief that orthostatic tolerance of subjects decreases dramatically if CEBR equals 0 or remains at the baseline level at the final stage of HDT.

Thus, the dynamics of changes in VP during HDT presented a distinct individual nature. The drop of VP by the end of the 2d month of the investigation should apparently be interpreted as a sign of adaptation to these conditions. One can assess the efficacy of preventive methods and agents, predict tolerance to orthostatic factors upon termination of HDT according to the dynamics of VP and CEBR.

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HUMAN HEART FUNCTION IN EARLY HOURS AND DAYS OF HEAD-DOWN TILT (ECHOCARDIOGRAPHIC DATA)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 2, Mar-Apr 86 (manuscript received 20 Nov 84) pp 42-46

[Article by V. V. Bystrov, A. F. Zhernavkov and A. A. Savilov]

[English abstract from source] Six healthy volunteers (aged 19-24) were exposed to head-down tilt (at 10°) for 7 days. The study revealed phasic changes of intracardiac circulation and the pump function which were not accompanied by contractility disorders. On the whole, the changes represented a manifestation of cardiovascular adaptation to hemodynamic shifts that are typical of this type of simulated weightlessness. The echocardiographic parameters varied similarly during the head-down tilt test and the joint Soviet-French experiment onboard Salyut-7.

[Text] Increasing use is being made in space medicine of the method of ultrasonic sounding of the heart--echocardiography [1, 2, 7, 18, 23].

Adoption of this method in medical support of spaceflights was preceded by investigation of human cardiovascular system function with simulation of weightlessness [2, 10, 11, 14, 16, 22, 24]. However, the results obtained thus far do not permit full identification of the mechanism of hemodynamic changes during man's adaptation to weightlessness. In particular, cardiac function in the first hours and days of simulated and real weightlessness requires further investigation. It is necessary to perform such work, in particular, for more accurate prediction of subsequent adaptation of the cardiovascular system to hemodynamic changes that arise.

Our objective here was to conduct more comprehensive studies than before [10, 11] of the changes in intracardiac hemodynamics, pumping and contractile function of the left ventricle during 7-day antiorthostatic hypokinesia (HDT, -10°). Special attention was devoted to investigation of the dynamics of the corresponding echocardiographic parameters in the first hours and days of submitting subjects to head-down tilt.

Methods

We examined 6 essentially healthy men 19-24 years of age. They were examined at physical rest 6 times on the 1st day of HDT, twice on the 2d day and once a day on the 3d-7th days of HDT.

The echocardiograms were recorded by conventional clinical methods [6, 9, 13, 17].

From the echocardiograms, we determined heart rate (HR), end diastolic and end systolic size of the left ventricle, diameter of the left atrium (DLA) and of the lumen of the root of the aorta, thickness of the posterior wall of the left ventricle (PWLV) and interventricular septum (IVS) in systole and diastole, excursion of PWLV, IVS and mitral valve movement, ejection period for blood from the left ventricle (EP).

We calculated end diastolic (EDV) and end systolic (ESV) volumes of the left ventricle [25], stroke (SV) and minute (CV) volumes of circulation, ejection fraction (EF), fraction of shortening of anteroposterior size of the left ventricle (SF) and rate of circulatory shortening of myocardial fibers (RCS).

The results were submitted to statistical processing using the paired non-parametric criterion of Wilcoxson [4].

Results and Discussion

During the 7 days of HDT, the subjects' general well-being was quite satisfactory, and no clinically significant signs of functional impairment of the heart were demonstrable.

Throughout the HDT period, HR was somewhat slower on the average ($p<0.05$) than in the baseline period. The most marked decline of HR (by 12%) was found on the 2d day of HDT. Examination on the 6th-7th days revealed a tendency toward normalization of this parameter (see Figure and Table).

Exposure of essentially healthy people with average physical development to HDT (-10°) for 7 days was not associated with appreciable changes in thickness or excursion of PWLV and IVS, or in nature and amplitude of movement of mitral valve cusps, diameter of the lumen of the root of the aorta or duration of EP.

At the same time, already in the first 2 h of HDT there was statistically reliable ($P<0.01$) increase in EDV and SV by an average of 6 and 10%, respectively. Starting in the 3d h and to the end of the 1st day of HDT, there was decline of these parameters to values slightly lower than the baseline, and this decline was statistically reliable ($P<0.01$) in comparison to values noted in the first 2 h of HDT.

On the 2d day of HDT there was a second, also reliable ($P<0.01$) increase in EDV and SV by a mean of 9-10%, which was associated with an increase in ESV by a mean of 8%. In this case, the increased ESV was apparently one of the manifestations of the heart's compensatory reaction, aimed at preventing

Dynamics of echocardiographic parameters during 7-day HDT (M±m)

Parameter	Base-line	Day of HDT												
		1, h					2, h							
		0	1	3	5	14	24	12	24	3	1	5	6	
HR/min	61,0±3,2	59,5±2,9	57,5±2,5	57,8±3,4	57,0±3,1	57,2±2,6	57,0±2,0	54,7±1,6	55,8±2,0	56,5±1,5	57,2±2,3	56,0±2,1	58,2±1,9	
EDV, ml	129,2±6,8	137,3±7,6	137,0±6,8	132,7±7,6	130,7±5,9	127,8±5,3	123,7±5,9	140,2±7,1	137,7±7,3	133,7±7,9	132,7±9,6	128,8±7,2	126,3±6,7	
ESV, ml	45,2±3,3	46,2±3,3	44,2±3,3	45,2±2,8	44,2±2,8	46,3±3,8	45,0±2,9	49,5±3,3	48,5±4,2	45,0±3,9	44,3±3,5	44,3±3,4	43,7±4,4	
SV, ml	84,0±5,7	91,2±6,6	92,8±4,8	87,5±5,6	86,5±3,7	81,5±4,0	78,7±3,9	90,7±5,2	89,2±5,0	88,7±3,4	88,2±7,7	84,5±5,9	82,7±4,1	
CV, ℓ/min	5,1±0,3	5,4±0,3	5,3±0,3	5,0±0,3	4,9±0,2	4,6±0,2	4,5±0,3	5,0±0,4	5,0±0,3	5,0±0,3	5,1±0,3	4,7±0,4	4,7±0,2	
EF, %	65,2±2,4	66,0±2,5	67,8±1,5	65,8±1,2	66,2±1,1	63,8±2,0	63,7±1,3	64,8±1,4	63,8±1,9	66,3±1,9	66,3±2,3	65,3±2,1	65,5±2,4	
SF, %	36,0±5,3	37,0±1,7	38,1±1,2	37,3±1,0	37,1±0,8	36,1±1,2	35,0±1,1	36,0±0,9	36,2±1,7	37,0±1,4	37,2±1,8	35,9±1,7	36,8±1,8	
RCS, s^{-1}	1,21±0,07	1,20±0,05	1,24±0,05	1,17±0,02	1,16±0,03	1,11±0,02	1,20±0,03	1,14±0,05	1,26±0,07	1,23±0,05	1,25±0,06	1,22±0,05	1,23±0,05	
DLA, cm	3,18±0,08	3,12±0,12	3,20±0,07	3,18±0,07	3,13±0,09	3,10±0,05	3,00±0,11	3,13±0,03	3,12±0,09	3,07±0,10	3,08±0,06	3,09±0,09	3,03±0,10	

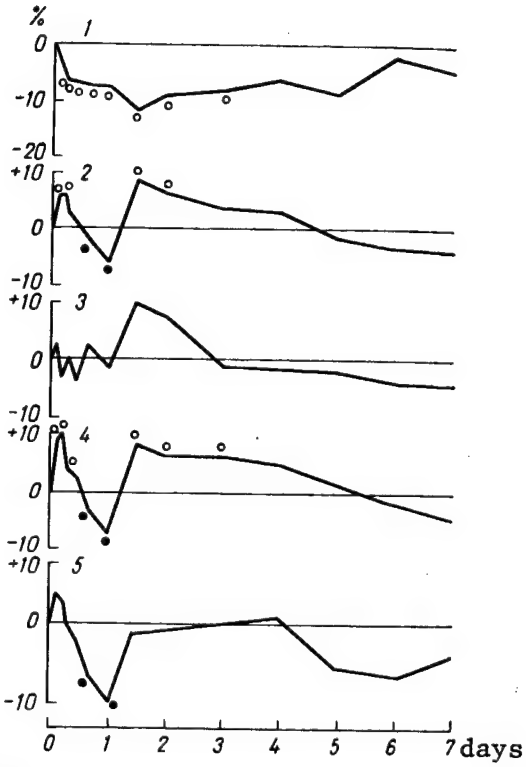
excessive increase in SV inadequate to prevailing conditions and, consequently in CV.

By the 4th-5th day of HDT, there was gradual return of mean EDV, ESV and SV to almost baseline values. At the end of the 7th day, the mean values of these echocardiographic parameters were even somewhat lower than in the baseline period.

The dynamics of mean CV were the same in direction as EDV and SV. However, in spite of the increase in EDV and SV, absolute CV (with exception of the first 3 h of HDT) did not differ appreciably or was 10-15% lower than the baseline, which was attributable to a significant degree to the stable decline of HR.

There were insignificant changes in mean DLA on the 7th day of HDT, and as a rule they corresponded to the changes in EDV, SV and CV. One could have expected somewhat greater increase in DLA, particularly right after submitting the subjects to HDT conditions, since it is expressly in this period that the most marked hemodynamic changes were observed, which were associated with increased venous return of blood to the heart. The absence of significant changes in DLA, i.e., its anteroposterior size, was probably related to the distinctions of change in configuration and hemodynamics of the left atrium and veins entering it with a relatively small volume load on the heart, as well as the limited capacities of one-dimensional echocardiography, which did not permit precise quantitative evaluation of volume of the left atrium with change in correlation between its transverse and longitudinal axes.

As also reported by other researchers [11, 14], the above-mentioned changes were not associated with appearance of electrocardiographic signs of



Changes in echocardiographic parameters during 7-day HDT (-10°); x-axis, days of HDT
1-5) HR, EDV, ESV, SV and CV, respectively
White and black circles--statistically reliable changes as compared to values recorded in first 2 h of HDT, respectively [sic]. Other designations are described in the text

impaired contractility of the myocardium. This was indicated, in particular, by the lack of marked changes in individual and mean values for EF, SF and RCS. However, since the echocardiographic examinations in this study were performed at relative physical rest, we cannot rule out entirely the possibility of development of early, discrete signs of impaired myocardial contractility during 7-day HDT.

Thus, the changes observed during HDT consisted mainly of changes in echocardiographic parameters of delivery of blood to the heart in systole and diastole, as well as pumping function of the heart. These changes occurred in phases: first there was increase in EDV, SV and CV right after subjects were submitted to HDT, a decrease in these parameters by the end of the 1st day of HDT, then a second, marked and longer lasting increase on the 2d-4th day of HDT followed by decrease toward the end of the period of investigation to levels that were slightly lower than the baseline.

The immediate cause of increased diastolic filling of the left ventricle and SV of the heart after submitting subjects to HDT is apparently redistribution of blood in a cranial direction and, consequently, increased venous return to the heart, as well as a corresponding change in pressure in its chambers and intrathoracic vessels [8, 15, 20, 21]. According to some authors, the extent of change in pressure in these vascular regions could be quite substantial in essentially healthy people. For example, in tests with HDT (-5° and -6°), the initial rise of central venous pressure (CVP) in the first 2 h reached 20-50% in subjects referable to a similar age group (26-27 years), whereas its drop, in relation to baseline values, in subsequent hours of the 1st day of HDT constituted 40-55%. The latter occurred against the background of increased diuresis and reduced volume of circulating blood [15, 21].

It should be noted that the changes in echocardiographic parameters demonstrated in the first 24 h of HDT coincided in time with development of the "phase of primary reactions" to real and simulated weightlessness, i.e., the period of search for optimum form of regulation of basic functions of the body [5]. In this period, there is the most marked redistribution and deposition of blood in vascular regions, greatest compensatory "dumping of fluid" and, consequently, decrease in circulating blood volume [3, 12, 19]. The secondary change in

volumetric echocardiographic parameters on the 2d-7th days of HDT coincided with development of the so-called "basic phase of adaptation," during which there is alteration of basic functions and activity of the body's regulatory systems in response to development of adaptive hemodynamic changes that are specific to real and simulated weightlessness [5].

A comparison of our findings here to the results of analogous echocardiographic studies conducted during the joint Soviet-French space mission enabled us to detect some similarity of direction of changes in the above-mentioned parameters of intracardiac hemodynamics and cardiac function in man during HDT and weightlessness. Just like we found in our subjects here, cosmonaut J.-L. Chretien showed phasic changes in basic echocardiographic parameters during weightlessness; in particular, a reliable increase in EDV and SV (3d-4th day of the mission, by 13 and 22%, respectively) was noted after an initial slight decline, then (by the 6th day of the mission) there was a second decline of these parameters to slightly less than preflight values. While there was the same direction as during HDT of changes, absolute CV values were considerably higher (by 30-40%) during the mission than in the preflight examination. However, this was attributable chiefly to persistent increase of HR at all stages of the examination in weightlessness. The latter is probably related to an appreciable extent to the nervous and emotional stress inherent in work under the extreme conditions of spaceflight, particularly since cosmonaut J.-L. Chretien participated actively in the echocardiographic studies.

It was previously shown that such increase in HR and CV is a typical distinction of the cardiovascular system's reaction to central redistribution of blood under HDT conditions in older individuals, such as J.-L. Chretien [15]. As in the case of HDT, the changes demonstrated in weightlessness in volumetric echocardiographic parameters were functional, they were consistent with the hemodynamic changes that developed on the 1st day of spaceflight and were not associated with appearance of signs of change in geometry of chambers of the heart, movement of its structures and impairment of myocardial contractility [23].

Considering the results of these investigations with HDT, it can be assumed that the increase in filling of the left ventricle and some intensification of pumping function during spaceflights occur not only on the 3d-4th day, as found in J.-L. Chretien, but at earlier stages of the flight, i.e., right after cosmonauts are submitted to weightlessness.

On the whole, our findings confirm the conception of adaptation of the human circulatory system to real and simulated weightlessness as an undulant process that undergoes specific stages of development. The changes in hemodynamics and cardiac function demonstrated in the early hours and days of HDT are apparently a manifestation of the initial compensatory (antiorthostatic) reaction to central redistribution of blood that is typical of this experimental model of weightlessness. According to an existing hypothesis, one of the principal mechanisms of this compensatory reaction is stimulation of reflexogenic baroreceptor zones of the heart, lungs and intrathoracic vessels, which leads to realization of the unloading reflexes aimed at normalization of pressure and blood flow in central and peripheral vessels [14].

It is desirable to take into consideration the distinct existence of phases in reactions of the human cardiovascular system to HDT and weightlessness when elaborating appropriate protective and preventive measures aimed at curbing increase in venous return to the heart and corresponding rush of blood to the head during flights. However, it is necessary to conduct analogous echocardiographic investigations during spaceflights, particularly, in the first hours and days after cosmonauts are submitted to weightlessness, in order to select optimum types of measures and times for their use. Such work would also settle the question of validity of extrapolating data obtained in ground-base studies with simulated weightlessness to spaceflight conditions.

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HUMAN BLOOD FREE AMINO ACIDS AT EARLY STAGE OF HEAD-DOWN TILT

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[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] The concentration of 17 free amino acids in plasma of 6 test subjects, aged 20, who were for 7 days exposed to head-down tilt and remained on a controlled diet, was measured. The study revealed an increase in the concentration of most amino acids by the end of day 3 and all amino acids by the end of day 7. This indicates that the diet used is a good source of the required amino acids and that there are processes which facilitate an increase of amino acids during the first days of exposure. The concentration of most amino acids returned to the baseline level on the 7th recovery day.

[Text] A number of authors, who made studies of healthy adult males submitted to long-term antiorthostatic hypokinesia (HDT) at -4° for a long time, found increase in concentrations of most free amino acids in samples of venous blood drawn on the 12th, 21st, 30th, 39th and 48th days of HDT [5]. It is interesting to measure amino acids at earlier stages of HDT.

We report here the results of a study of levels of 17 free amino acids in blood plasma of subjects at the early stages of HDT, with the head tilted at an angle of -10°, who were kept on the cosmonaut diet.

Methods

Investigation of levels of 17 free amino acids in plasma during HDT at 10° was conducted with the participation of 6 healthy men 20 years of age. Samples of venous blood were drawn in the morning, on a fasting stomach, in the baseline period, at the end of the 3d and 7th days of HDT, as well as on the 7th day of the recovery period.

After processing the samples using a standard method [1, 2], amino acid concentration in plasma was assayed with a Hitachi automatic analyzer (model KLA-3B) that operated on the principle of ion-exchange chromatography. Margin of error of the method was ±2%.

The subjects received ordinary food on standard menus in the baseline and recovery periods; however, their actual food intake fluctuated in the following range: baseline (1 day before HDT): 115.2±9.4 g protein (including 57.2 g of animal origin), 519.8±34.8 g carbohydrate, 178.1±12.8 g fat, with a total caloric value of 4090.4±166 kcal; in the recovery period, the figures were: 105.9±11.7 g (63.6 g), 328±31.1 and 155.1±10.1 g, respectively, totaling 3041.9±238 kcal.

During HDT, the subjects were given the standard daily food allowance for cosmonauts. Actual intake was 118.24±5.4 g protein, 389.1±16.1 g carbohydrate and 101.82±6.2 g fat totaling 2794.88±137 kcal.

Table 1. Free amino acids of subjects' plasma in baseline period (mg%)

Amino acid	Subject						Group mean concentration (M±m)	Individual fluctuations	Range of individual fluct., mg%	Adult men
	Il-o	M-y	N-y	V-v	G-v	P-v				
Essential amino acids										
Lysine	3,41	3,25	3,29	3,38	3,47	3,52	3,38±0,04	3,25 - 3,52	0,27	3,65±0,06
Valine	2,31	2,28	2,27	2,19	2,17	2,14	2,22±0,02	2,14 - 2,31	0,17	2,33±0,02
Threonine	3,51	3,48	3,49	3,58	3,56	3,66	3,54±0,02	3,48 - 3,66	0,18	1,94±0,03
Methionine	0,26	0,30	0,31	0,33	0,28	0,29	0,29±0,009	0,26 - 0,33	0,07	0,33±0,00
Leucine	1,43	1,40	1,49	1,56	1,53	1,51	1,48±0,02	1,40 - 1,56	0,16	1,60±0,02
Isoleucine	0,70	0,81	0,73	0,79	0,75	0,68	0,74±0,02	0,68 - 0,81	0,13	0,82±0,01
Phenylalanine	1,17	1,14	1,14	1,06	1,21	1,07	1,13±0,02	1,06 - 1,21	0,15	0,88±0,01
Total EA	12,79	12,66	12,72	12,89	12,97	12,87	12,81±0,04	12,66 - 12,89	0,23	11,55±0,06
Nonessential amino acids										
Cystine	1,10	1,12	1,05	1,00	1,07	1,14	1,08±0,02	1,00 - 1,14	0,14	0,75±0,01
Tyrosine	1,18	1,27	1,16	1,21	1,12	1,25	1,19±0,02	1,12±1,27	0,15	0,92±0,01
Alanine	2,27	2,41	2,29	2,39	2,18	2,16	2,28±0,04	2,16 - 2,41	0,25	2,84±0,04
Arginine	1,49	1,51	1,57	1,44	1,47	1,62	1,51±0,02	1,44 - 1,62	0,18	1,33±0,02
Aspartic acid	0,12	0,14	0,13	0,13	0,13	0,13	0,13±0,00	0,12 - 0,14	0,02	0,29±0,07
Histidine	1,05	1,20	1,18	1,27	1,19	1,24	1,18±0,03	1,05 - 1,27	0,22	1,12±0,01
Glycine	1,38	1,39	1,25	1,43	1,44	1,31	1,36±0,02	1,25 - 1,44	0,19	1,46±0,02
Glutamic acid	3,58	3,50	3,49	3,36	3,42	3,56	3,48±0,03	3,36 - 3,56	0,20	4,13±0,05
Proline	2,03	2,10	2,11	2,00	2,14	2,16	2,09±0,02	2,00 - 2,16	0,16	2,25±0,02
Serine	1,92	1,86	1,84	1,79	1,88	1,90	1,86±0,01	1,79 - 1,90	0,11	1,51±0,02
Total NA	16,12	16,50	16,07	16,02	16,04	16,47	16,02±0,02	16,50 - 16,02	0,48	16,60±0,01
Total amino acids	28,91	29,16	28,79	28,91	29,01	29,34	28,83±0,02	28,79 - 29,34	0,55	28,15±0,06
EA/NA ratio	0,79	0,77	0,79	0,80	0,81	0,78	0,79±0,01	0,77 - 0,81	0,04	0,69±0,03

Results and Discussion

In the baseline period, when the subjects followed their usual routine and ate the usual food, plasma levels of the essential amino acids (EA) valine, lysine, methionine, leucine and isoleucine were slightly below mean normal values obtained previously [3] in a study of 124 healthy men in most of our subjects (Table 1). At the same time phenylalanine and threonine concentrations (particularly the latter) exceeded these mean values. Apparently,

the relatively higher concentrations of phenylalanine and threonine in all subjects were attributable to the specific life style, diet and metabolic distinctions of individuals whose growth processes had not yet stopped (all of the subjects were 20 years of age), which were inherent in all of them. The high levels of plasma phenylalanine and threonine resulted in a higher total EA than the mean for this parameter obtained in [3]. A. S. Ushakov and T. F. Vlasova [5] measured mean concentrations of valine, methionine, leucine and isoleucine in plasma of 80 healthy adult men of an older age, and they exceeded the levels of these amino acids in our subjects. Conversely, lysine and particularly threonine concentrations were higher in our subjects.

Only the concentration of isoleucine was within the range of physiological fluctuations [4] in all of the subjects, and in 5 out of the 6 cases, so was leucine. Lysine, threonine and phenylalanine levels exceeded the top of the physiological range, while methionine content was below the bottom of the physiological range in 5 out of 6, and that of valine was below the physiological range in half of these cases.

Nonessential amino acid (NA)--alanine, aspartic and glutamic acids, glycine and proline--levels in plasma were lower in the baseline period than the means found previously in a screening of 124 adult men (see Table 1). The concentrations of cystine, tyrosine, arginine and serine was above these means in all subjects and histidine level was above them in most cases. Total NA content of plasma was somewhat lower in all subjects than the normal mean [3]. The higher total of EA concentrations and, on the contrary, lower total EA resulted in a higher value for the EA/NA ratio in our subjects, as compared to the means for this parameter (see Table 1) obtained in [3].

According to data published in [5], plasma levels in our subjects of NA--alanine, aspartic and glutamic acids, histidine, glycine and proline--were also lower than the norm, while arginine level was higher [5]. Cystine, tyrosine and serine concentrations were close to this norm [5].

In all of our subjects, tyrosine, arginine, histidine, glycine and proline content was within the range of physiological fluctuations cited in [4], while serine, aspartic and glutamic acid content exceeded the top of the range. Alanine concentration was lower in all our cases than the parameters cited in [4].

Thus, in the baseline period, the EA, valine and methionine, were present in lower concentrations than the mean normal values given in [2, 5] and the bottom of the physiological range of fluctuations given in [4]. Although the concentrations of leucine and isoleucine were below the mean "norm," they were within the physiological range of fluctuations cited in [4] in most of our subjects. According to [2, 4, 5], concentrations of threonine, phenylalanine and lysine exceeded both the mean norm of the cited authors and the top of the range of physiological fluctuations. The concentrations of most EA, which differed from mean normal values listed in [2, 5], were within the range of physiological fluctuations [4]. Only the concentration of alanine was below the bottom of the range of physiological fluctuations.

Table 2. Levels of free amino acids in subjects' plasma after 3 days of HDT and use of cosmonaut diet

Amino acid [AA]	Subject						Mean group concentration (M±m)	Individual fluctuations	Range of fluct. mg%	Changes in relation to baseline status	
	Il-o	M-y	N-y	V-ov	G-v	Pr-v				mg%	%
Essential amino acids											
Valine	2,75	2,65	2,63	2,48	2,57	2,51	2,60±0,04	2,51—2,76	0,25	+0,38*	+17,75
Lysine	4,48	4,39	4,51	4,56	4,62	4,68	4,54±0,04	4,39—4,68	0,29	+1,16*	+35,69
Threonine	4,38	4,51	4,61	4,69	4,72	4,75	4,61±0,05	4,38—4,75	0,37	+1,07*	+30,74
Methionine	0,39	0,38	0,44	0,43	0,36	0,41	0,40±0,01	0,36—0,44	0,08	+0,11*	—42,30
Leucine	2,51	2,36	2,26	2,40	2,28	2,18	2,33±0,04	2,18—2,51	0,33	+0,85*	+60,71
Isoleucine	0,92	0,79	0,88	0,86	0,84	0,84	0,85±0,01	0,79—0,92	0,13	+0,11*	+16,17
Phenylalanine	1,20	1,26	1,21	1,17	1,18	1,13	1,19±0,01	1,13—1,26	0,13	+0,06**	+5,66
Total EA	16,64	16,34	16,54	16,59	16,57	16,50	16,53±0,04	16,34—16,64	0,30	+3,72*	+29,38
Nonessential amino acids											
Cystine	1,50	1,36	1,31	1,44	1,54	1,53	1,44±0,03	1,31—1,54	0,23	+0,36*	+36,00
Tyrosine	1,21	1,22	1,16	1,27	1,24	1,20	1,21±0,01	1,16—1,27	0,11	+0,02*	+1,78
Alanine	2,18	2,45	2,43	2,29	2,38	2,24	2,32±0,04	2,18—2,45	0,27	+0,04*	+1,85
Arginine	1,92	1,70	1,86	1,64	1,61	1,51	1,70±0,06	1,51—1,92	0,21	+0,69***	+47,91
Aspartic acid	0,14	0,12	0,19	0,17	0,18	0,16	0,16±0,01	0,12—0,19	0,07	+0,03***	+25,0
Histidine	1,45	1,54	1,38	1,39	1,38	1,34	1,41±0,02	1,34—1,54	0,20	+0,23*	+21,90
Glycine	1,30	1,37	1,29	1,26	1,41	1,35	1,33±0,02	1,26—1,37	0,11	—0,03*	—2,40
Glutamic acid	4,69	4,60	4,31	4,39	4,48	4,57	4,50±0,05	4,31—4,69	0,38	+1,12*	+33,33
Proline	2,36	2,38	2,44	2,29	2,40	2,50	2,39±0,02	2,29—2,50	0,21	+0,30*	+15,09
Serine	2,97	3,10	3,16	2,92	3,00	3,05	3,03±0,03	2,92—3,16	0,24	+1,17*	+65,39
Total NA	19,72	19,84	19,53	20,06	19,62	19,45	19,70±0,09	19,45—20,06	0,61	+4,09*	+31,58
Total AA	36,36	36,18	36,07	36,65	36,19	35,95	36,06±0,10	39,95—36,65	0,70	+7,63*	+29,55
EA/NA ratio	0,84	0,82	0,85	0,83	0,84	0,85	0,83±0,004	0,82—0,85	—	—	—

* $P < 0,001$. ** $P < 0,05$. *** $P < 0,02$.

Table 2 lists the results of assaying plasma amino acid levels in our subjects in the morning, on a fasting stomach, at the start of 4 days of HDT. First of all, we are impressed by the increase, as compared to the baseline, in concentrations of valine, lysine, threonine, methionine, leucine, cystine, histidine, glutamic acid, proline and serine in all subjects. Concentrations of isoleucine, phenylalanine, arginine and aspartic acid increased in 5 out of 6 cases, i.e., in most subjects. Glycine concentration increased somewhat in only 2 cases, in the rest its absolute value decreased. As compared to the baseline average group status, the increase in concentrations of all amino acids, with the exception of tyrosine, alanine and glycine, was reliable ($P<0.001$) and exceeded the margin of error of the method, which constituted 2%. Concentrations of tyrosine, alanine and glycine were virtually retained at the baseline. There was less significant increase in concentration of phenylalanine (+5.7%). Among the EA, the greatest increases in relation to the baseline period were referable to leucine (61%), methionine (42%), lysine (36%), threonine (31%), and among the NA, to serine (65%), arginine (48%), cystine (36%), glutamic acid (25%) and histidine (22%).

On the 4th day of HDT, the group mean concentrations of most amino acids were above the mean "normal" values obtained in [3], and only the mean concentration of isoleucine corresponded to the mean level, while aspartic acid and glycine levels were lower than in the baseline period. The sum of EA and NA, as well as total amino acid content, were higher on the 4th day of HDT than in [3].

If we analyze the individual data, we can conclude that the concentrations of valine, lysine, threonine, methionine, leucine, phenylalanine, cystine, tyrosine, arginine, histidine, serine and glutamic acid were above the mean "norm" cited in [3] in all our subjects. Special mention should be made of the high concentrations of such amino acids as threonine, lysine, leucine, phenylalanine, cystine, histidine, glutamic acid, serine and (to a lesser extent) tyrosine and arginine. In most subjects, the concentrations of isoleucine and proline were also above the mean "normal" values. In all of our subjects, only the concentrations of alanine, aspartic acid and glycine were below the mean for that "norm" [3].

Thus, the supply of such amino acids as valine, lysine, methionine, leucine, isoleucine, proline, aspartic and glutamic acids improved in 3 days of HDT with use of cosmonaut diet, as compared to the baseline status of the subjects ($P<0.001$). The concentrations of these amino acids, which were low in the baseline period, became higher than the "norm" [3]. As for such amino acids as threonine, phenylalanine, cystine, arginine, serine, histidine, the baseline levels of which exceeded the means in [3], their supply increased in the subjects. Supply of tyrosine remained at the same mean level. Only plasma alanine and glycine content remained at virtually the baseline level, which was lower than the means found in [3].

A comparison of our data to the parameters of A. S. Ushakov and T. F. Vlasova [5] revealed that, in our subjects, plasma concentrations of leucine, lysine, threonine, cystine, tyrosine, arginine, serine and glutamic acid after 3 days of HDT exceeded the mean "norm," valine and phenylalanine levels corresponded to this norm, while isoleucine, methionine, alanine, aspartic acid, histidine, glycine and proline concentrations were lower. Thus, according to that norm

[5], we observed improvement of supply of only such amino acids as leucine and cystine, arginine, serine and glutamic acid.

In spite of the noted changes that occurred in plasma amino acid content, by the start of the 4th day of HDT the concentrations of most amino acids remained in the range of the physiological fluctuations indicated in [4]. Plasma levels of lysine, threonine, phenylalanine, serine and glutamic acid were above their top "normal" range [4]. However, the concentration of alanine was lower. Consequently, the supply of methionine and valine increased in our subjects, while that of alanine remained low.

Table 3 lists data on plasma amino acid content after 7 days of HDT. According to the data listed there, in this period the concentrations of all amino acids, both as the mean for the group ($P<0.001$) and each subject individually, were higher than in the baseline period (with consideration of margin of error of the method--2%). Accordingly, the sum of EA and NA was greater ($P<0.001$). As compared to the status after 3 days of HDT, there was continued increase in concentrations of valine, lysine, methionine, isoleucine, phenylalanine, histidine and aspartic acid. There was also an increase by this time in concentrations of tyrosine, alanine and glycine, which had been at virtually the baseline level after 3 days of HDT. At the same time, as compared to the status after 3-day HDT, there was relative decrease in concentrations of threonine, leucine, cystine, arginine, serine and glutamic acid. Proline concentration remained at the same level. Total EA increased, while NA remained at the same level. Total amino acids remained the same (with consideration of 2% margin of error of the method). As compared to the baseline period, the greatest increase among EA was referable to lysine (by 49%), methionine (48%), leucine (46%), threonine (27%), isoleucine (22%), valine (21%) and among the NA, this applied to serine (50.5%), aspartic acid (46%), histidine (41%), cystine (30%) and glutamic acid (28%).

Table 4 lists plasma amino acid levels 7 days after HDT. In the recovery period, the concentrations of most amino acids were lower than in the baseline period, or else they reverted to the initial level: valine 5%, lysine 8.9%, threonine 9.6% ($P<0.001$), tyrosine 12.6%, histidine 32%, glutamic acid 21% ($P<0.001$). Relatively higher concentrations than in the baseline period persisted for methionine (+17%)($P<0.01$), leucine (+8%, $P<0.001$), isoleucine (+4%, $P>0.05$), aspartic acid (+38%, $P<0.001$). On the whole, the sum of EA ($P<0.001$) and sum of NA ($P>0.05$) were lower than in the baseline period. As compared to the status after 7-day HDT, there was substantial decrease in the recovery period in concentrations of all amino acids, particularly lysine, histidine, serine, aspartic and glutamic acids. Alanine decreases the least.

In the recovery period, plasma concentrations of valine, lysine, isoleucine, alanine, glycine, proline, aspartic and glutamic acids were below the mean "norm" indicated in [3] in all of the subjects as they were in the baseline period. The concentrations of threonine, phenylalanine, arginine, cystine, tyrosine and serine were, as in the baseline period, above the mean values of the cited "norm." In the recovery period the concentrations of methionine and leucine conformed to the mean values for the "norm" cited in [3], unlike the baseline period, when their supply was low in the body.

Table 3. Plasma free amino acid content in subjects after 7 days of HDT on cosmonaut diet (mg%)

Amino acid [AA]	Subject						Mean group concentration (M±m)	Individual fluctuat. in group, mg%	Range of individual fluctuat., mg%	Change in relation to baseline	
	Il-o	M-y	N-y	V-v	G-v	Pr-v				mg%	%
Essential amino acids											
Valine	2,71	2,73	2,69	2,66	2,64	2,75	2,69±0,01	2,64—2,75	0,11	−0,47	−21,2
Lysine	5,07	4,97	4,92	4,86	5,12	5,37	5,04±0,07	4,86—5,37	0,51	+1,6	+49,1
Threonine	4,52	4,66	4,38	4,58	4,63	4,24	4,50±0,06	4,24—4,58	0,34	−0,96	−27,1
Methionine	0,44	0,47	0,40	0,39	0,48	0,43	0,43±0,01	0,39—0,48	0,09	+0,14	+48,3
Leucine	2,08	2,17	2,13	2,29	2,30	2,04	2,16±0,04	2,04—2,30	0,26	+0,68	+45,9
Isoleucine	0,85	0,93	0,92	0,87	0,97	0,87	0,90±0,01	0,85—0,93	0,08	+0,16	+21,6
Phenylalanine	1,25	1,28	1,22	1,30	1,31	1,29	1,27±0,01	1,22—1,31	0,09	+0,14	+12,4
Total EA	16,86	17,21	16,66	16,95	17,45	16,99	17,02±0,11	16,86—17,45	0,59	+4,21	+32,9
Nonessential amino acids											
Cystine	1,52	1,40	1,36	1,37	1,33	1,44	1,40±0,02	1,33—1,52	0,19	+0,32	−20,5
Tyrosine	1,41	1,29	1,38	1,35	1,35	1,34	1,35±0,01	1,29—1,41	0,12	+0,16	−13,3
Alanine	2,60	2,47	2,54	2,49	2,58	2,66	2,55±0,02	2,47—2,66	0,19	+0,27	−11,8
Arginine	1,82	1,75	1,74	1,68	1,78	1,77	1,75±0,01	1,68—1,82	0,14	+0,24	−15,9
Aspartic acid	0,34	0,31	0,25	0,29	0,38	0,37	0,32±0,02	0,25—0,37	0,12	+0,19	+146,1
Histidine	1,70	1,62	1,69	1,76	1,49	1,72	1,66±0,03	1,49—1,76	0,27	−0,48	−40,7
Glycine	1,63	1,49	1,59	1,72	1,56	1,61	1,60±0,03	1,49—1,72	0,23	+0,24	−17,6
Glutamic acid	4,51	4,54	4,29	4,45	4,58	4,32	4,44±0,04	4,29—4,58	0,29	+0,96	+27,7
Proline	2,46	2,41	2,51	2,39	2,46	2,19	2,40±0,04	2,19—2,51	0,32	−0,31	−14,8
Serine	2,88	2,73	2,91	2,92	2,80	2,60	2,80±0,05	2,60—2,92	0,32	+0,94	−50,5
Total NA	20,87	20,01	20,26	20,42	20,31	20,02	20,31±0,12	20,01—20,87	0,86	+4,70	−30,1
Total AA	37,73	37,22	36,92	37,37	37,76	37,01	37,33±0,14	36,92—37,76	0,84	−8,90	−31,3
EA/NA ratio	0,81	0,86	0,82	0,83	0,86	0,85	0,83±0,008	0,81—0,86	0,05	—	—

*P<0.001 for all amino acids.

Table 4. Plasma free amino acid content in recovery period (mg%)

Amino acid	Subject						Mean group concentration (M±m)	Individual fluctuat. in group, mg%	Range of individual fluctuat. mg%	Change from baseline mg%	Change from baseline %	Change by 7th day of HDT
	Il-o	M-y	N-y	V-v	G-v	P-v						
	Essential amino acids											
Valine	2,07	2,18	2,10	2,15	2,14	2,02	2,11±0,02	2,02—2,18	0,16	—0,11*	—5,0	—21,6
Lysine	2,77	2,66	2,84	2,92	2,85	2,86	2,81±0,03	2,66—2,92	0,26	—0,72**	—8,9	—44,2
Threonine	3,21	3,12	3,18	3,15	3,26	3,28	3,20±0,02	3,12—3,28	0,16	—0,34**	—9,6	—28,9
Methionine	0,35	0,39	0,34	0,33	0,30	0,37	0,34±0,01	0,30—0,39	0,09	+0,05*	+17,2	—20,9
Leucine	1,64	1,69	1,58	1,57	1,53	1,62	1,60±0,02	1,53—1,69	0,16	+0,12**	+8,1	—25,9
Isoleucine	0,81	0,83	0,79	0,75	0,77	0,72	0,77±0,01	0,72—0,83	0,11	+0,03*	+4,1	—14,5
Phenylalanine	1,04	1,16	1,10	1,18	1,24	0,87	1,09±0,05	0,87—1,24	0,37	—0,04*	—3,5	—14,2
Total EA	11,89	12,03	11,93	12,05	12,09	11,74	11,95±0,05	11,74—12,09	0,35	—0,86**	—6,8	—29,8
	Nonessential amino acids											
Cystine	0,99	1,06	1,12	1,10	1,03	1,01	1,05±0,02	0,99—1,12	0,13	—0,03	—2,8	—25
Tyrosine	1,05	1,03	0,99	1,12	1,18	0,92	1,04±0,03	0,92—1,18	0,26	—0,15**	—12,6	—23
Alanine	2,29	2,30	2,31	2,36	2,27	2,48	2,33±0,03	2,27—2,48	0,21	+0,05	+2,2	—8,6
Arginine	1,48	1,54	1,46	1,51	1,43	1,56	1,49±0,02	1,43—1,56	0,13	—0,02	—1,3	—4,9
Aspartic acid	0,21	0,19	0,17	0,15	0,20	0,19	0,18±0,008	0,15—0,21	0,06	+0,05**	+38,5	—43,8
Histidine	0,79	0,85	0,82	0,73	0,88	0,76	0,80±0,02	0,73—0,88	0,15	—0,38**	—32,2	—51,8
Glycine	1,29	1,28	1,36	1,31	1,45	1,47	1,36±0,03	1,28—1,47	0,19	0	0	—15
Glutamic acid	2,63	2,79	2,84	2,68	2,81	2,75	2,75±0,03	2,63—2,84	0,21	—0,73**	—21	—31,8
Proline	2,11	2,00	2,14	2,08	2,17	2,21	2,11±0,03	2,00—2,21	0,21	+0,02**	+6,9	—12,1
Serine	1,83	1,76	1,90	1,97	1,79	1,96	1,86±0,03	1,76—1,96	0,20	0	0	—33,6
Total NA	15,58	14,8	15,11	15,01	15,21	15,31	15,17±0,10	14,8—15,58	0,78	—0,5	—2,8	—25,3
Total AA	27,47	26,83	27,04	27,06	27,3	27,05	27,12±0,09	26,83—27,47	0,64	—1,71***	—4,6	—22,4
EA/NA ratio	0,76	0,81	0,79	0,80	0,79	0,77	0,78±0,007	0,76—0,81	0,05	—	—	—

* $P<0,001$. ** $P<0,0001$. *** $P<0,05$.

Thus, plasma levels of amino acids on the 8th day of the recovery period corresponded essentially to the baseline status.

The results of these studies warrant the conclusion that, already at the early stage of -10° HDT, there was reliable increase in concentrations of most free amino acids in all of the subjects. This could be due to a set of factors: excessive intake of amino acids with food, as compared to metabolic requirements, decreased intensity of protein synthesis under hypokinetic conditions, development of catabolic processes in muscle tissues associated with breakdown of proteins, signs of stress of immobilization, increase in plasma amino acid concentrations related to signs of dehydration in the acute period of adaptation to HDT.

After 7-day HDT, high levels of all amino acids in plasma persisted, as compared to the baseline status. However, as compared to the status after 3-day HDT, not all amino acids demonstrated an increase. There was continued increase in concentrations of valine, lysine, methionine, isoleucine, phenylalanine, histidine and aspartic acid. As compared to the baseline period, there was increase in concentrations of tyrosine, alanine and glycine, the levels of which in plasma presented a mild tendency toward elevation in the first 3 days. The concentration of proline held at a level that was close to the value on the 3d day of HDT, although it was higher than in the baseline period. Plasma levels of threonine, leucine, cystine, arginine, serine and glutamic acid dropped somewhat in 7 days of HDT, as compared to the status at the beginning of the 4th day, but remained higher than the baseline. The impression is gained that, in this period, factors causing elevation of amino acid levels in the subjects' plasma continued to be active. We refer, first of all, to the relatively excessive food intake, slower protein synthesis and catabolic processes. Interestingly, in this period there was increase in concentrations of amino acids, the levels of which changed little in the first 3 days.

We were impressed by the fact that, by the end of the 7th day of HDT, the process of increase in most amino acids became overtly less intensive than in the period of the first 3 days of HDT. For seven amino acids, the process was even reversed: decrease or stabilization of concentrations. In analyzing this phenomenon, it should be borne in mind that, by the end of the 7th day of HDT, the process of dehydration slowed down, the negative nitrogen balance diminished, the subjects had already adapted to the new conditions and felt better. At this time, they consumed more of their food allowance.

Thus, the greatest change in amino acid content, as compared to the baseline status, occurred in the first 3 days of HDT.

The findings were different in the recovery period: we observed a process of decrease in plasma levels of all amino acids, as compared to the status at the end of the 7th day of HDT; concentrations of most amino acids returned to their baseline values. In this period, food intake was no longer excessive, as it had been during HDT, there was prevalence of anabolic processes related to recovery of muscle tissue; intensity of protein synthesis increased; hypokinesia-caused stress was no longer present.

It is desirable to take into consideration the demonstrated dynamics of amino acid metabolism during adaptation to HDT conditions when elaborating food allowances for cosmonauts. In particular, the plasma amino acid levels are indicative of a large supply of protein in the body from food intake during the period of adaptation to HDT, which suggests that protein content in the diet could be reduced when relevant indications are present.

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BLOOD SERUM ENZYME ACTIVITY IN HEALTHY MAN WITH SIMULATION OF EFFECTS OF WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by I. A. Popova]

[English abstract from source] The enzymic activity of blood of healthy male volunteers was examined during 8-day bed rest in the horizontal and head-down (-6°) position, water immersion up to the neck and 6-hour head-down tilt (-15°). Alkaline phosphatase, cholinesterase (CE), leucine arylamidase (LA), glutamate dehydrogenase (GDH) and gamma-glutamyl transpeptidase (GGTP) were measured. During horizontal bed rest the activities of all the enzymes, except for GDH, decreased in a moderate degree which was very distinct at an early stage of exposure. The activity of GDH and CE decreased significantly after the exposure. The enzymic activity tended to decline during head-down tilt at -6°. The LA and GGTP activity decreased to a greater extent, being statistically significant during head-down tilt at -6° and in the recovery period. The enzymic activity insignificantly increased during water immersion and 6-hour head-down tilt at -15°, remaining in some cases elevated during 5 days after exposure. The lower activity of enzymes (which was significant for some of them) during horizontal and antiorthostatic bed rest was primarily associated with diminished motor activity, whereas increased enzymic activity was related to the gravity-induced blood shift to the intrathoracic area.

[Text] Examination of blood serum activity is practiced widely as a biological diagnostic test for evaluation of health status. Not only pathological states, but adaptive processes when the body is exposed to extreme factors are based on change in enzyme activity or their coordinated function.

Examination of cosmonauts before and after space missions revealed changes in activity of some enzymes after both long- and short-term flights [2, 3].

Performance of biochemical tests only before and after flights makes it difficult to gain precise information about the effects of different spaceflight factors on man due to the fact that there is some summation of effects.

Our objective here was to examine the activity of blood serum enzymes in healthy subjects in the presence of states simulating the effect of weightlessness.

Methods

The effects of weightlessness with its inherent gravity-induced redistribution of blood were simulated by short-term bedrest (BR) in horizontal and antiorthostatic [head-down tilt] (-6°, HDT) positions, dry immersion in a water environment up to the neck and brief (up to 6 h) HDT (-15°).

The investigations were conducted with the participation of healthy male subjects 31-40 years of age, with height of 170-185 cm and weight of 65-87.5 kg. Duration of BR and water immersion (WI) did not exceed 8 days. Blood was drawn in the morning, on a fasting stomach, from the ulnar vein with the subjects supine. It was tested 2-3 times before exposure to above factors, 3-5 times during exposure and 2-3 times in the recovery period (RP). The times of blood tests and number of subjects in each experiment are listed in Tables 1-4.

The following enzymes were assayed in blood serum: alkaline phosphatase (EC 3.1.3.1; AP), cholinesterase (EC 3.1.1.7; CE), leucine arylamidase (EC 3.4.11; LA), L-γ-glutamyl transpeptidase (EC 2.3.2.2; GGTP), glutamate dehydrogenase (EC 1.4.1.3; GLDH). Enzyme activity was determined by enzymospectrophotometric or colorimetric methods using standard commercial sets of Beringer reagents.

The material was submitted to statistical processing by the method of comparison of conjugate variants using Student's criterion.

Results and Discussion

According to the data listed in Table 1, BR in horizontal position did not elicit appreciable changes in activity of the tested serum enzymes for 7 days. However, most of them (with the exception of GLDH) presented a tendency toward decrease in activity, particularly at the early stages of BR. For LA, this decline was statistically reliable on the 2d day of BR. A reliable decrease in CE and GLDH activity in blood serum was demonstrable on the 2d and 7th days of BR, respectively.

Table 1. Human blood serum enzyme activity (in IU/ℓ) during BR in horizontal position (M±m); n = 5)

Enzyme	Before BR	Day of BR			Day after BR	
		2	4	7	2	7
AP	103,9±8,4	99,6±19,2	102,0±17,3	103,9±17,2	98,0±14,2	100,0±17,4
CE	2958±143	2667±131	2814±110	2712±112	2375±95*	2718±159
LA	19,5±1,3	15,5±0,7*	17,0±1,2	16,3±2,0	15,2±2,3	15,8±1,7
GGTP	28,0±5,0	22,4±5,9	21,9±6,6	22,0±5,6	21,1±5,2	20,1±4,7
GLDH	2,2±0,5	2,5±0,4	2,6±0,6	2,1±0,5	1,9±0,4	1,2±0,3*

Note: Here and in Tables 2-4, n refers to number of cases; asterisk indicates $P<0.05$.

Table 2. Human blood serum enzyme activity (IU/ℓ) during HDT (-6°)

Enzyme	Statistical parameter	Before HDT	Day of HDT					Day after HDT		
			2	4	6	7	8	2	3	7
AP	*M*	106,6	111,2	108,7	106,4	115,5	110,0	109,2	110,2	106,2
	m	4,3	8,3	7,4	9,0	15,5	13,7	10,5	9,5	10,5
	n	26	10	11	6	5	6	5	6	5
CE	*M*	2583	2322	2568	2465	2425	2593	2240	2358	2302
	m	113	135	162	189	220	153	236	261	125
	n	27	10	11	6	5	6	5	6	5
LA	*M*	15,4	13,3	13,1	12,1*	14,8	12,7*	13,5	12,5*	14,4
	m	0,9	0,9	0,8	1,1	1,4	1,0	0,6	0,9	0,9
	n	26	10	11	6	5	6	5	6	5
GGTP	*M*	18,9	11,9*	12,3*	—	11,7*	—	12,6*	—	12,1*
	m	1,9	1,1	1,1		0,8		0,9		0,8
	n	5	5	5		5		5		5
GLDH	*M*	1,3	1,3	1,4		1,6		1,6		1,6
	m	0,2	0,3	0,3		0,2		0,2		0,2
	n	5	5	5		5		5		5

During BR with HDT (-6°), there was essentially retention of the tendency toward decrease in blood enzyme activity. In some cases the differences were more distinct than during BR in horizontal position. Thus, with HDT, the decline in LA activity was statistically reliable on the 6th and 8th days of HDT and on the 3d day of BR, while GGTP decline was statistically reliable throughout the period of HDT and BR (see Table 2).

Intensification of the effects of gravity-induced redistribution of blood by using a larger tilt angle in HDT (see Table 3) did not, however, lead to noticeable changes in blood enzyme activity. Most enzymes presented a mild tendency toward increased activity after 3 and 6 h of exposure and upon its termination.

Table 3. Blood serum enzyme activity (IU/ℓ) during HDT (-15°)(M±m; n = 5)

Enzyme	Before HDT	HDT, h		After HDT	
		3	6	30 min	1 day
AP	123,4±8,5	128,7±9,5	128,7±9,7	128,7±8,1	126,7±10,2
CE	3186±139	3486±162	3327±175	3425±156	3247±157
GGTP	27,8±5,2	29,9±5,0	29,0±5,6	30,3±5,3	26,9±4,5
GLDH	4,1±0,9	4,4±1,6	3,3±0,6	2,9±0,6	2,6±0,6

During WI (up to the neck), we also failed to demonstrate substantial changes in activity of blood serum enzymes (see Table 4), in spite of the fact that there were significant hemodynamic shifts and changes in fluid-electrolyte balance and systems of its regulation [8]. During WI, as with 6-h HDT (-15°), blood enzyme activity increased insignificantly (unreliably). A high level of activity persisted in most of the tested enzymes for 5 days after exposure.

Table 4. Human blood serum enzyme activity (IU/ℓ) during WI up to the neck in seated position

Enzyme	Statist. param.	Before WI	Day of WI					Day after WI		
			2	4	6	7	8	2	3	5
AP	*M*	101,9	105,5	108,3	100,1	103,4	108,9	118,2	97,3	114,9
	m	4,2	8,5	7,0	7,6	15,7	10,0	9,3	7,0	10,2
	n	22	12	12	6	6	6	6	4	6
CE	*M*	2527	2625	2742	2586	2463	2586	2510	2401	2452
	m	122	171	202	302	428	306	303	170	207
	n	22	12	12	6	6	6	6	4	6
LA	*M*	13,3	14,0	14,0	13,6	14,4	14,2	14,4	15,9*	15,3
	m	0,5	0,5	0,5	0,7	0,5	0,9	1,5	1,0	0,7
	n	22	12	12	7	6	6	6	3	6
GGTP	*M*	13,4	13,6	13,9	11,9	14,1	12,4	14,6	12,7	15,8
	m	1,1	1,6	1,5	0,6	3,1	0,7	2,6	1,6	2,3
	n	20	11	11	5	6	5	6	3	6

Among the changes that appeared with exposure to the experimental factors, two factors were of prime significance: diminished voluntary motor activity; redistribution of blood and tissue fluid from the legs to the upper part of the body. Emotional reactions also played some part.

The dynamics demonstrated in this study of blood serum activity during BR, HDT and WI indicate that none of the above-mentioned factors simulating the effects of weightlessness has an appreciable influence on level of blood enzyme activity. The insignificant decrease in blood enzyme activity during BR and HDT could be due most to restriction of motor activity. In this state, the intensity of tissue metabolism could be diminished because of decreased expenditure of energy. It is known that the activity of many enzymes, of both tissues [7, 9] and blood [4, 5] increases with extreme physical loads.

While hypokinesia leads to decrease in activity of some blood enzymes, gravity-induced redistribution of blood to the intrathoracic region, which is inherent in antiorthostatic positions and occurs in weightlessness, apparently causes development of hyperenzymemia. Under the conditions of our investigation (i.e., with moderate angles of inclination of the head end of the body and brief HDT and WI), the observed increase in blood enzyme activity was mild, but it was inherent in all of the tested enzymes. The latter leads us to assume that hyperenzymemia, which occurs with gravity-induced redistribution of blood, may be attributable to a decreased volume of circulating plasma. According to a number of authors [1, 6], circulating blood volume decreases after 24-h HDT by 420-425 mℓ, which is about 8% of total blood volume. The increase in blood enzyme activity during HDT constituted a mean of 4.4-9.4%.

Dry submersion into a water immersion environment (up to the neck) leads to more significant hemodynamic changes. During WI, about 700 mℓ blood shifts to the thoracic region [8]. On this basis, we should have expected more marked changes in blood enzyme activity during WI than we demonstrated in this study. Apparently, the maximum increase in enzyme activity during WI is compensated by opposite changes induced by immobilization. This is confirmed by the fact that maximum changes were noted after WI, but even

in this case, maximum increase in blood enzyme activity did not exceed 15.9% for AP, 17.9% for GGTP and 19.5% for LA.

During an actual spaceflight, when gravity-induced redistribution of blood is not associated with a decrease in intensity of voluntary movements, there can be more distinct manifestation of increase in blood enzyme activity.

It was previously reported that cosmonauts presented increased activity of many blood enzymes, among which the most noticeable changes were referable to creatine kinase (CK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and GGTP, on the 1st day after short-term space missions. After the first 4 missions aboard the reusable transport spacecraft, the Space Shuttle, astronauts presented an increase in activity of CK, LDH and GGTP by a mean of 34.5, 21.1 and 18.1%, respectively [2]. In our studies, which were pursued after 8-day spaceflights, we observed a significant increase in activity of CK and AST in blood by 109.8 and 25.9%, respectively. The greater manifestation of hyperenzymemia following real spaceflights than in model experiments confirms the hypothesis we expounded above that the blood redistribution factor is very significant to the genesis of hyperenzymemia demonstrated in cosmonauts. However, we cannot rule out a different explanation. Perhaps, in addition to shifts of blood volume, there are other mechanisms that lead to increase in blood enzyme activity after spaceflights, in particular, stress factors.

Our findings are indicative of the possible role of gravity-induced redistribution of blood in onset of dysenzymemia in cosmonauts as well, but they do not enable us to conclude that the changes in blood enzyme activity are entirely identical during real spaceflights and simulation of weightlessness. This stresses the need to search for more adequate models or to conduct tests aboard space vehicles.

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PARAMECIUM TEST FOR TOXIC SUBSTANCES IN HUMAN BLOOD DURING SIMULATED WEIGHTLESSNESS

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[Article by V. I. Lavrov, I. B. Goncharov, A. F. Davydkin, A. P. Ivanov, A. N. Romanov and V. F. Ivchenko]

[English abstract from source] The Paramecium test was for the first time used to measure the buildup of toxic substances in the healthy man exposed to simulated weightlessness. The most distinct changes were seen on bed rest days 3 and 7-8 in all test subjects (41 subjects). After bed rest day 8 the parameter reached a plateau, the toxicity level stopped to increase, but the Paramecium test time remained shorter than normal. It can therefore be suggested that the prognosis of any disease that may develop in this situation will be worse. In view of this it is important to improve the prophylaxis and treatment of endogenous and exogenous intoxications during spaceflight and to provide active detoxication based on the purification of biological fluids by sorption.

[Text] It is known that long-term hypokinesia elicits functional disturbances in various organs and systems of the body: microcirculation [1] is involved, all types of metabolism change [10], there is increase in blood triglycerides and nonesterified fatty acids [4, 10], other incompletely oxidized products accumulate [6, 3], there is a higher probability of onset of diseases associated with intoxication.

For this reason, the question of using detoxification measures when rendering medical aid at different stages of spaceflights is quite timely.

At the present time, hemadsorption is one of the most effective detoxification methods. At the same time, it is the simplest, in comparison to others. Apparently, it can be used at low and zero gravity. In clinical practice, hemadsorption is used extensively and with success in combined therapy of both acute diseases associated with intoxication [5, 7, 11] and exogenous poisoning of diverse etiology [9].

Change in "toxicity" of plasma, which is determined with the Paramecium test, is an integral indicator of accumulation of toxic products in the body.

Our objective here was to investigate the dynamics of the Paramecium test in essentially healthy people submitted to antiorthostatic hypokinesia (HDT) and immersion as the most popular models of weightlessness.

Methods

We used the Paramecium test developed by V. S. Genes et al. [2] as a method for determining the "toxicity" of plasma. We applied 0.01 mℓ plasma to a slide and an aliquot of suspension containing 6-10 Paramecia, then both drops were thoroughly mixed. Determination was made of time of death of all cells. The specimen was tested 3 times and mean data were used [8]. As a control, we determined the life span of Paramecia in plasma of healthy people, which averaged 24-25 min [8].

We examined the dynamics of change in the Paramecium test [PT] in 41 essentially healthy men 25 to 45 years of age. All of the subjects were divided into 5 groups: the 1st consisted of 9 men submitted to HDT (-8°) for 7 days; the 2d, 9 subjects who spent 14 days in HDT (-8°) position; the 3d, 6 subjects submitted to immersion for 7 days (by the method of dry, unsupported submersion) [12]; the 4th, 9 men in HDT, -8°, position for 14 days; 5th, 8 men who were also submitted to -8° HDT for 14 days. In each group, the PT was performed in the baseline period, on the 3d, 7th, 14th days of HDT, on the 1st, 3d, 7th day of immersion, as well as on the 3d day of the recovery period. In the 5th group, the PT was performed daily. The results were submitted to mathematical processing for each group separately. The differences were statistically reliable.

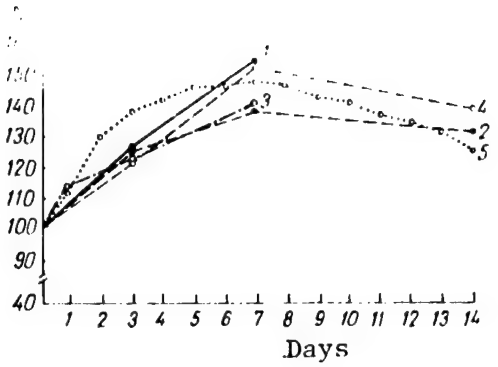
Results and Discussion

In the 1st group, the baseline PT constituted 26 min 26 s±44.9 s. By the 3d day of HDT, PT showed 19 min 29 s±65 s, by the 7th day of HDT, life span of Paramecia in plasma decreased to 14 min 48 s±47.9 s. On the 3d day of the recovery period, this parameter constituted 17 min 19 s±44.5 s.

In the 2d group of subjects, life span of Paramecia in plasma in the baseline period constituted 22 min 50 s±69 s. By the 3d day of HDT it decreased to 17 min 30 s±28.9 s. On the 7th day of hypokinesia, the PT showed 12 min 12 s; by the 14th day of HDT, this parameter rose to 14 min 45 s±89 s and on the 3d day of the recovery period it was 17 min 40 s±37.6 s.

In the 3d group, the time in the PT constituted 24 min 40 s±47.1 s in the baseline period. By the end of the 1st day of immersion life span of Paramecia decreased to 21 min 58 s±70 s, and by the 3d day this parameter constituted 20 min 30 s±39.6 s. The most significant changes were demonstrated on the 7th day of immersion--16 min 25 s±29.7 s. By the 3d day of the recovery period, this test was in the normal range, 22 min 51 s±38.3 s.

In the 4th group of subjects, life span of Paramecia constituted 21 min 46 s± 43.2 s in the baseline period; by the 3d day of HDT this parameter decreased to 16 min 21 s±55 s, and by the 7th day to 13 min 51 s ±29.6 s. By the end of



Dynamics of change in "toxicity" of plasma according to PT in subjects submitted to HDT and immersion

X-axis, days of HDT; y-axis, toxicity (%)

1-5) 1st-5th groups, respectively

the 14th day of HDT, the PT constituted 15 min 45s±12.6 s, and on the 3d day of the recovery period, 20 min 22s± 55.2 s.

The dynamics of changes in the PT in the 5th group of subjects can be seen distinctly on the graph (see Figure).

Changes in the PT were in the same direction in all five groups of subjects. They were the most significant in the acute stage of adaptation and on the 7th day of HDT and immersion. It is expressly at this time that there are the most acute processes of adaptation. Interestingly, there was some increase in life span of Paramecia in the period following the 7th day of hypokinesia and it held on a distinctive "plateau" by the 14th day of HDT. By this time, the body had virtually adapted to hypokinetic conditions, and vital functions became stabilized on a new level. Apparently, this affected the integral indicator of accumulation of toxic properties in blood, although it did not remain at above the baseline level.

The fact that there was significant decline in PT time as an integral indicator of accumulation of toxic agents in the human body during model experiments must be taken into consideration with onset of acute diseases in operators during spaceflights. Accumulation in blood of toxic products as a manifestation of compensatory and adaptive reaction of the body to adverse factors present during spaceflights does not, of course, in itself require detoxification measures aboard a spacecraft. But, in the case of onset of disease in an operator, the presence of toxic agents in his blood could have an adverse effect on course and prognosis.

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TYPOLOGICAL CHARACTERISTICS OF CENTRAL HEMODYNAMICS OF MONKEYS IN CLINOSTATIC AND ORTHOSTATIC POSITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by A. N. Demin, G. S. Belkaniya and V. A. Dartsmeliya]

[English abstract from source] By tetrapolar rheography central hemodynamics was investigated in 74 rhesus monkeys in the clino- and orthostatic state. The basic hemodynamic parameters were examined in relation to the entire sample, to the group with a higher or lower blood pressure (BP_{mean}) and to four states of central circulation in orthostatic animals. The typological circulatory differences in the orthostatic state were shown to be determined by qualitatively different hemodynamic mechanisms responsible for BP_{mean}. The hemodynamic characteristics in the clino- and orthostatic state were found to be reciprocally related. It is recommended to take into consideration the typological differences of hemodynamics that can modify cardiovascular responses to various effects.

[Text] Orthostatic circulatory insufficiency is one of the main biological consequences of man's exposure to weightlessness in the course of long-term hypokinesia [4, 7, 10, 14, 15].

For this reason, investigation of the mechanisms of hemodynamic regulation in orthostatic position (OP) and development on this basis of recommendations for prevention of orthostatic disorders constitute a timely direction of investigation in clinical and experimental medicine. Comparative physiological investigations yield basic general biological information; as for extrapolation of experimental data to man, when selecting the object of investigation one should be governed by the principle of concrete morphological and functional consistency. Adherence to this principle is particularly important when studying orthostatic reactions of the cardiovascular system. It is only in man and animals that can stand erect that about 70% of the blood is localized below the level of the heart. In quadrupeds, conversely, about 70% of the blood is concentrated at or above the level of the heart [16]. This basic difference in hemodynamic situation is the reason for qualitative differences in reactive distinctions and mechanisms of regulation of the cardiovascular system of

primates, as compared to quadrupeds used the most often in experiments (dogs, cats, rabbits, rats, etc.). In particular, this is also indicated by the higher orthostatic stability of monkeys, as compared to other animals [1].

Our objective here was to examine the basic parameters of central hemodynamics of monkeys, the semi-erect and erect positions of which determine well-developed antigravity function in this species [1].

Methods

Studies were conducted on 74 Macaca rhesus males 1 to 8 years of age weighing 1.5-11 kg. Parameters of central hemodynamics during the orthostatic test, which was performed on a turntable, were determined using a modification of the method of tetrapolar thoracic rheography [2]. Rheograms were recorded on an RPG2-02 rheoplethysmograph.

For analysis, we used indexed (scaled to body weight) parameters of central hemodynamics: stroke index (SI, $m\ell \cdot kg^{-1}$), cardiac index (CI, $m\ell \cdot kg^{-1}$), specific peripheral vascular resistance (SPR, $dyne \cdot s \cdot cm^{-5}$). Systolic ($BP_s$) and diastolic ($BP_d$) arterial pressure were measured by the Korotkov method. Mean pressure was calculated using the formula: $BP_m = BP_d + 0.42(BP_s - BP_d)$. Heart rate (HR) was determined from the rheogram. Amplitude of the differential rheogram (A_{dif}, $\Omega \cdot s^{-1}$) was used as an indicator of myocardial contractility [12, 13].

Hemodynamic parameters were recorded in clinostatic position (CP) and for 1-5, 10, 15 and 20 min of subsequent orthostatic testing. The changes in parameters considered were evaluated as a percentage of CP.

Results and Discussion

Dynamics of orthostatic changes in monkeys presented phasic changes in the main hemodynamic parameters (Figure 1). Parameters in the 1st-5th min reflect the influence of the hydrostatic factor, which is compensated in some cases, in the 1st-2d min, by the animal's psychoemotional response to change in position of the body. On the whole, dynamics of parameters from the 1st to 10th min characterize a transient process of triggering of the mechanism of compensation for the hydrostatic factor, whereas parameters in the 10th-20th min reflect stabilization of function of mechanisms regulating the cardiovascular system. Absence of reliable changes in mean values of parameters in the 10th, 15th and 20th min is indicative of relative stabilization of hemodynamics. For this reason, we used averaged values of the main hemodynamic parameters in the 10th, 15th and 20th min of OP as the statistical characteristic of the different parameters.

According to the total sample (see Table) BP_m in the course of the selected times of orthostatic testing were below baseline values in clinostatic position, constituting 96 ± 2.2 and $94 \pm 2.3\%$ of the baseline, respectively. It should be noted that the relative changes in BP_m ranged from a 38% drop to 16% rise in different animals, as compared to the baseline in CP. The general distinction of orthostatic reactions of different monkeys was 13 and 14% increase, respectively in HR in the transitory period and period of stabilized hemodynamics.

As can be seen in Figure 1 and the Table, in monkeys in OP in the general sample (A), there was decrease in cardiac output: SI decreased by 37% and CI by 26%, while SPR increased by 4% in the 10th-20th min.

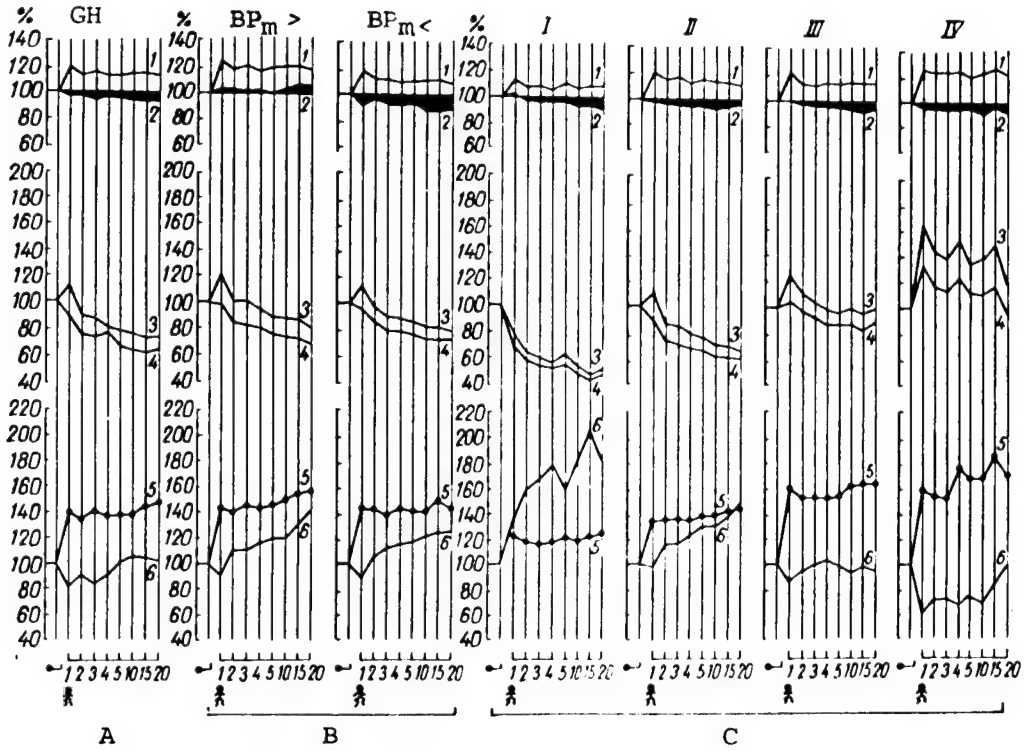

Figure 1. Dynamics of changes in main parameters of central hemodynamics of monkeys in OP. X-axis, testing time (min); here and in Figure 2, Roman numerals indicate type of hemodynamics

A) total sample
B) groups with rise (>) and drop (<) of BP_m
C) according to type of hemodynamics

GH) general hemodynamics
1) HR
2) BP_m
3) CI
4) SI
5) A_{dif}
6) SPR

It should be noted that, in addition to quantitative differences there were also qualitatively different hemodynamic reactions in OP according to the changes in level of BP_m. Thus, in some animals BP_m exceeded the baseline level in CP, whereas in others it was considerably lower throughout the orthostatic test period. There is information in the literature about classification of orthostatic reactions, in particular in monkeys [1], on the basis of nature of changes in BP_m and HR. However, reliable differences were not demonstrable in cats with respect to changes in stroke volume in groups formed according to direction of changes in BP_m [11]. In other investigations [8, 9], such comparison was not made. For this reason, we analyzed the distinctions of basic hemodynamic parameters of monkeys divided into two groups, one with high and the other with low BP_m in OP.

As can be seen in Figure 1B, classification of orthostatic reactions according to rise or drop of BP_m failed to demonstrate distinctions of hemodynamic mechanisms of maintaining BP_m with use of this factor. Indicators of the dynamics

of changes in SI, CI and SPR in the two groups were in the same direction and did not differ reliably, with the exception of HR which was reliably higher ($P<0.01$) in the group with elevated BP_m. This indicates that it is inexpedient to use changes in BP_m as a classifying criterion. BP_m is a finite controllable parameter, and for this reason the mechanisms involved in regulating it (cardiac output, peripheral resistance of vessels, circulating blood volume, etc.) are ambiguously reflected in BP_m characteristics, although expressly they determine the qualitative distinctions of hemodynamic regulation in OP. We were impressed by the fact that the main parameters of central hemodynamics changed over a wider range in different animals than BP_m and HR. For example, SI in OP ranged from 38 to 163% in relation to baseline in CP, CI ranged from 40 to 194% and SPR from 4 to 188%. This suggests that the typological characteristics of hemodynamics in OP on the basis of change in cardiac output reflect more objectively the heterogeneous mechanisms of maintaining BP_m.

Central hemodynamic parameters as related to main types of circulation in monkeys in OP

Parameter	Total sample	Type of hemodynamics in OP			
		I	II	III	IV
BP_m:					
A	115±2,1	116±6,0	110±3,0	120±3,8	117±7,9
B	96±2,2	97±2,1	96±1,4	97±1,9	96±6,0
C	94±2,3	93±2,5	94±2,0	92±3,5	96±6,0
SI:					
A	2,1±0,19	2,75±0,3	2,41±0,3	1,33±0,19	1,34±0,4
B	77±8,4	59±2,7	75±3,3	94±4,0	109±10,0
C	63±7,7	48±2,5	62±2,0	86±3,0	109±10,0
CI:					
A	427±37,9	631±68	526±70	285±42	234±84
B	89±9,0	64±3,6	88±3,6	107±5,0	136±10,0
C	74±9,0	51±2,5	69±1,8	98±3,0	136±10,0
SPR:					
A	39 449±4917	16 965±2112	27 520±5716	45 210±4851	89 559±6812
B	90±9,0	157±9,8	116±5,2	95±4,6	74±8,3
C	104±10,3	190±12,7	138±5,0	95±4,3	74±8,3
HR:					
A	210±4,4	235±11,0	211±6,0	211±7,0	183±6,0
B	114±1,8	108±3,6	116±2,4	114±2,8	127±7,0
C	113±2,0	107±4,0	113±2,8	114±2,0	127±7,0
A_{dif}:					
A	2,97±0,14	4,16±0,26	3,29±0,21	2,5±0,14	1,76±0,37
B	139±4,0	120±8,1	136±4,0	155±5,6	175±17,0
C	144±4,0	122±8,2	141±4,5	163±5,3	175±17,0

Key: A) absolute values in CP
B,C) mean values in 1st-5th and 10th-20th min of OP, respectively (% of baseline in CP taken as 100%)

The main types of hemodynamics in OP were identified on the basis of evaluation of the direction of changes in cardiac output in relation to CP. Hemodynamics in OP, where CI held at the level of the confidence range of baseline CP values (from 84 to 116%) were defined as eukinetic (type III). With the hyperkinetic or IV type of hemodynamics, cardiac output was reliably higher than in CP (CI>116%). When CI in OP dropped below 84% of the baseline in CP, a hypokinetic state was identified, in which types II (84% > CI > 68%) and I (CI < 68%) were distinguished. With the qualitatively same direction of changes in CI, separation of hypokinetic circulation in OP into types I and II

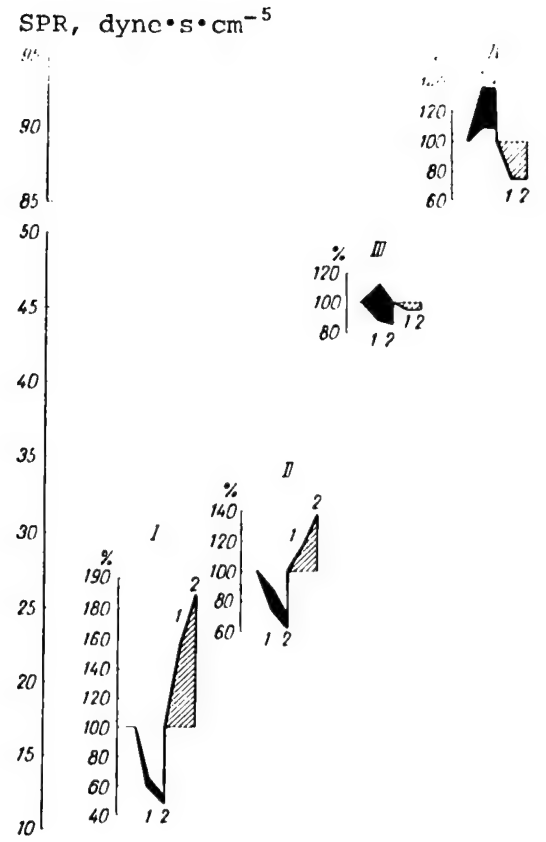

Figure 2.
Phase relationships between main hemodynamic states (types I-IV) in monkeys in OP

Interpretation of graphic profile of hemodynamic state: top and bottom edges of black field--relative level of SI and CI, respectively; striped field--relative changes in SPR (% of baseline in CP) in transitory period (1) and period of stabilized hemodynamics (2) in OP. Levels of profile location correspond to absolute SPR in CP. Y-axis--SPR (dyne•s•cm^{-5}; thousands)

was made arbitrarily in order to single out the extreme state (type I) characterized by marked (mean of 50%) decrease in cardiac output. The statistical characteristics of the hemodynamic states determined by the main circulatory parameters are listed in the Table. The hemodynamic types or states of circulation in OP were distributed as follows in frequency of occurrence: type I--15%, II--40%, III--33% and IV--12%.

Hemodynamic states in OP presented no reliable differences in BP_m or HR increment, but they reflected well the qualitative differences in mechanisms of maintaining systemic BP. Thus, with a hypokinetic circulatory state in OP, maximum decline of cardiac output is compensated by the most marked increase in peripheral vascular resistance: by 90% with type I hemodynamics and 38% with type II. Systemic pressure was maintained in a hypokinetic circulatory state in OP (types I and II) primarily by means of peripheral vasoconstriction. Hyperkinetic hemodynamics in OP (type IV) are obtained due to the cardiac component, which is manifested by intensification of inotropic myocardial function (amplitude of differential rheogram increases by 75%) and relatively greater HR increment (by 27%) in the presence of decrease (by 26%) in peripheral vascular resistance. With a eukinetic state of hemodynamics in OP (type III), there are intermediate changes in peripheral vascular resistance and inotropic myocardial function.

We were impressed by the distinctive "reciprocal" relationship between hemodynamic characteristics of monkeys in CP and OP, which had been previously reported in humans [5, 6]. With hypokinetic hemodynamics in OP (particularly with type I), characterized by maximum decline of cardiac output and maximum increment of SPR, highest CI and lowest SPR are demonstrable in CP. The reverse was demonstrable with the hyperkinetic type of circulation (see Table). On the whole, however, the change from type I to type IV in OP is associated with reliable decrease in cardiac output ($P<0.001$) and corresponding progressive buildup of peripheral vascular resistance ($P<0.001$) in CP (Figure 2). There

are grounds to believe that the demonstrated distinct direction of change in relationship between baseline CI and SPR in CP and their change in OP apparently reflects successive phase states in regulation of circulation [3, 5, 6]. The general direction of compensation for the orthostatic factor is optimization of central circulation, as reflected by the successive change from hypokinetic to formation of hyperkinetic hemodynamics in OP. This is associated with progressive fixation of systemic increase in peripheral vascular resistance in the clinostatic state. Figure 2 shows well the transition from hypokinetic (type I) to hyperkinetic (type IV) hemodynamics in OP through successively increasing corresponding baseline levels of peripheral vascular resistance in CP.

Thus, these studies of primates revealed distinct typological distinctions of central hemodynamics and demonstrated opposite relations between basic parameters of circulation in CP and OP. In evaluating reactivity of the cardiovascular system, one should be governed by typological distinctions that could modify significantly reactivity of the cardiovascular system to various factors, rather than general statistical characteristics of hemodynamic parameters.

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DISTINCTIONS OF CAPILLARIZATION OF WHITE RAT SKELETAL MUSCLE DURING ADAPTATION TO HIGH ALTITUDE OF THE PAMIRS AND ANTARCTICA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 2, Mar-Apr 86 (manuscript received 20 Aug 84) pp 65-69

[Article by V. Sh. Belkin and O. B. Astakhov]

[English abstract from source] The capillary-myofiber quantitative relations were examined morphometrically in 180 white male rats exposed for 1.5 month to altitudes of 3488-4000 m above sea level (Antarctic and Pamir highlands). During the first three weeks of adaptation drastic changes in the parameter were seen. It is suggested that one of the factors responsible for them is a shift in the functional status of muscles produced by the method of transportation of the animals to the highland environment.

[Text] The effect on the body of the set of factors prevailing at high altitudes is a special concern of physicians and biologists in different special fields. However, there are rather limited publications dealing with adaptation to high-altitude conditions [5, 6, 8], and there are virtually no data about Antarctica. We submit here comparative data obtained in a study of morphological changes in vascular and tissular elements of white rat skeletal muscle in the course of adaptation to the high-altitude conditions of the Pamirs and Antarctica.

Methods

This study was conducted on 180 mongrel white male rats weighing 140-160 g. Investigations were pursued in Dushanbe (control--810 m above sea level), in the Northwestern Pamirs (Fortambek glacier, 4000 m above sea level) and in Central Antarctica (Vostok Station, 3488 m above sea level). At all stages of the experiment, the rats were kept in standard cages at room temperature of 19-22°C, they were fed pellet feed No 1. The animals were decapitated on the 1st, 3d, 7th, 14th, 21st, 28th and 41st-45th days at the high altitude (10 animals at a time). We excised pieces of muscle from the distal third of the head of the quadriceps, and they were fixed in 10% neutral formalin with subsequent preparation of histological specimens stained with hematoxylin and eosin, and after Van Gieson. Morphometric examination of capillarization of muscles was performed on histological preparations of

muscles with capillaries perfused with India ink by the method of S. M. Blinkov, and G. D. Moiseyev [4]. Determination was made of quantity of capillaries and muscle fibers per mm^2 section surface, total length of capillaries and muscle fibers per mm^3 tissue (μm), diameter of capillaries and muscle fibers (μm), volume of capillaries and muscle fibers per mm^3 tissue (μm^3), parameter characterizing the ratio of capillary volume to muscle fiber volume per mm^3 (%), quantity of capillaries per muscle fiber. The obtained digital material was submitted to variation statistical processing.

Results and Discussion

Capillarization of quadriceps in the Pamirs. One day after the animals were taken to an altitude of 4000 m above sea level, histological preparations revealed marked friability of connective tissue surrounding arterial and venous vessels of medium caliber, spasm of isolated arteries with a "palisade" of endothelial cells and vacuolization of smooth-muscle elements of the arterial wall. Among the muscle fibers there were areas of myocytes with focal disappearance of transverse markings.

Morphological evaluation of muscular capillarization (Figure 1) at this time revealed, along with dramatic increase ($P<0.01$) in diameter of the capillary lumen, decrease in their density per mm^2 muscle section surface ($P<0.01$). There was also a decrease ($P<0.05$) in mean number of capillaries per muscle fiber (3.40±0.15, versus 4.08±0.38 in the control). In spite of the increase in overall volume of capillaries per mm^3 tissue, these findings are indicative of worsening of conditions of nutrition of each muscle fiber.

At subsequent observation times (3d-14th day at high altitude), histological preparations demonstrated further development of morphological signs of impaired circulation. There were isolated fibers with signs of disappearance of transverse markings, fragmentation and clumped disintegration. On several preparations, there were focal accumulations of densely arranged lymphoid cells in connective tissue layers of the muscle (Figure 2).

Starting on the 3d day, there was increase in density of capillaries per mm^2 section surface. Concurrently with high indicators for diameter of capillary lumen, there was increase in total length of capillaries per mm^3 tissue (due to drastic tortuosity), which led to appreciable increase in overall volume of capillaries per mm^3 tissue (0.0500±0.0012 μm^3 on the 3d day, 0.046±0.006 μm^3 on the 7th and 0.051±0.066 μm^3 on the 14th day, versus 0.025±0.0014 μm^3 in the control). Maximum value for the parameter characterizing the ratio of capillary volume to volume of muscle fibers was demonstrated on the 14th day at high altitude (see Figure 1).

At subsequent observation times (21st-45th days), histological sections showed focal friability of perivascular connective tissue, total disappearance of foci of dystrophic and necrobiotic lesions to myocytes, in the presence of uneven plethora of the veins. Morphometric observations indicated that there was relative stabilization of parameters of capillarization on a new level. This is confirmed by the appreciable increase (as compared to the control) in diameter of capillary lumen and overall volume of capillaries per mm^3 tissue (see Figure 1).

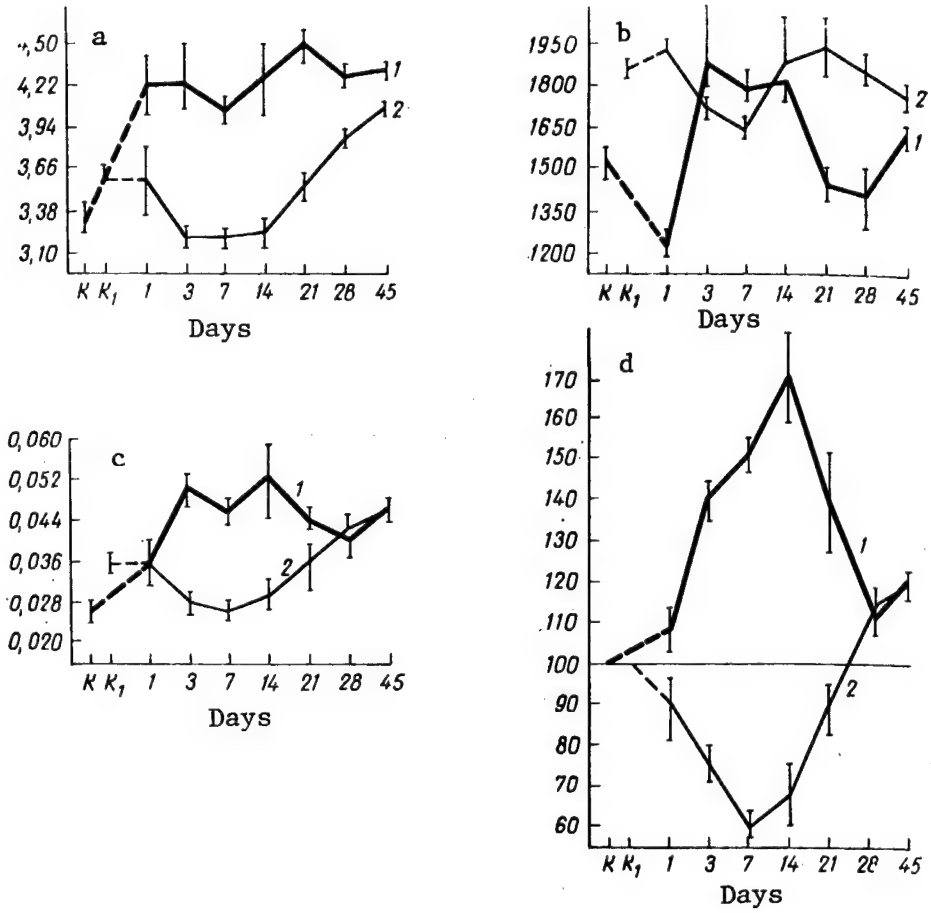

Figure 1. Dynamics of morphometric parameters of capillarization of white rat quadriceps during adaptation to high altitudes of the Pamirs (1) and Antarctica (2)

a) capillary diameter (μm)
b) number of capillaries per mm^2 section surface
c) total volume of capillaries (mm^3)
d) ratio of volume of capillaries to volume of muscle fibers (%)
K) control in Dushanbe
K_1) antarctic background

Capillarization of quadriceps at high altitude of Antarctica. It was established that, in spite of the relatively small difference between the absolute altitudes of Vostok Station and Fortambek glacier (512 m), the dynamics of capillarization of skeletal muscles in these two experiments differed drastically. In particular, skeletal muscles of animals decapitated in the first 3 weeks at the Vostok Station presented virtually similar tissue changes. Histological preparations of skeletal muscles (on 1st-21st days) revealed drastic inconsistency between severity of tissular and vascular disturbances. We observed "mosaic" dystrophic and necrobiotic lesions in the form of disappearance of transverse striation of muscle fibers, signs of

fragmentation and lumpy disintegration, manifested mainly in fibers with small and medium diameter (Figure 3). In the intramuscular blood stream, such changes as focal dilatation and plethora of capillaries, uneven plethora of veins, focal arterial spasm, edema of the stroma and perivascular edema were not diffusely distributed, and they were usually demonstrable around isolated areas of damage to muscle fibers.

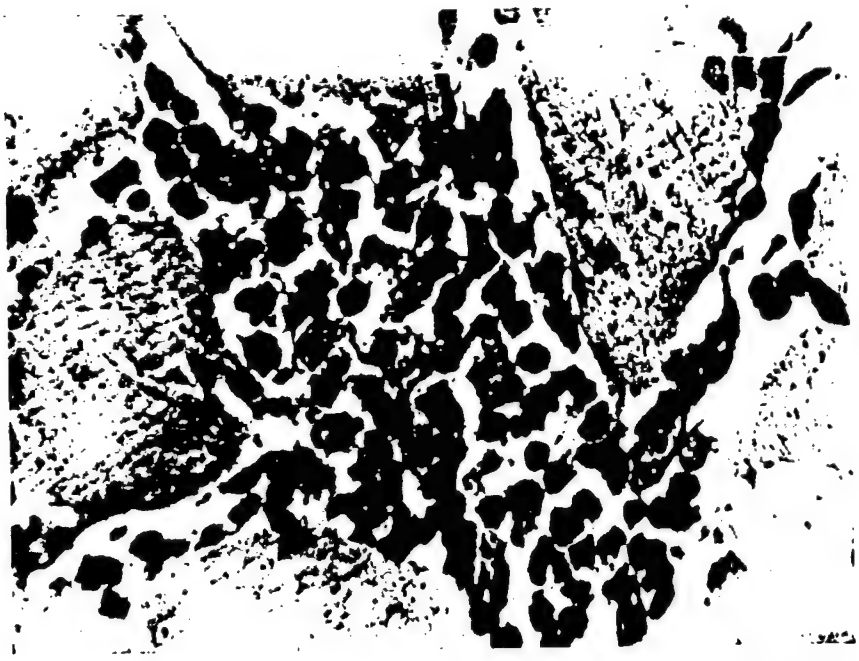

Figure 2. Focal polymorphic cell infiltration in connective tissue layers of white rat quadriceps on 14th day at 4000 m above sea level. Histological preparation. Hematoxylin and eosin stain. Magnification 200×

Morphological examination revealed substantial decline of parameters of capillary diameter and total volume per unit quadriceps volume on the 3d, 7th and 14th days. The decrease in capillarization at these times was confirmed by the corresponding change in mean number of capillaries per muscle fiber (as compared to Antarctic background). Of course, these conditions of vascularization of skeletal muscles did not reflect the actual oxygen requirement necessary for normalization of the developed tissue changes.

The distinctions of skeletal muscle capillarization at subsequent stages of adaptation to the high altitude in Antarctica (28th-41st days) constituted the next stage of adaptation of the intraorganic bloodstream of muscles to hypoxia, and they are indicative of its active role in regulation of circulation and redistribution of blood in the body. Signs of uneven plethora persisted against a background of receding tissular disorders. The increase in capillary diameter combined with high density of capillaries per mm^2 was manifested by an increase in overall volume per mm^3 tissue. These data, along with the increase in mean number of capillaries per muscle fiber, as well as

parameters of radius of diffusion which settled on the level of the baseline background, are indicative of improved capillarization of the tested skeletal muscles.

Figure 3. Dilated venules investing myocytes with signs of fragmentation. White rat quadriceps on 7th day at altitude of 3488 m above sea level. Histological preparation. Injection of blood vessels with black India ink. Hematoxylin and eosin stain. Magnification 400×

Figure 1 illustrates the main differences in dynamics of skeletal muscle capillarization during adaptation of white rats to high-altitude conditions of the Pamirs and Antarctica on the example of change in such an integral indicator as ratio of volume of capillaries to volume of muscle fibers per mm^3 tissue. There are dramatic differences in this parameter for the first 3 weeks of adaptation, and they are virtually the same on the 28th-41st days at high altitude.

Thus, our findings indicate that the dynamics of skeletal muscle capillarization differ drastically in animals adapting to the high-altitude hypoxia of the Fortambek glacier and Vostok Station. In animals delivered to Antarctica (Antarctic background), parameters of quadriceps capillarization reliably exceeded analogous parameters obtained on animals decapited in Dushanbe (see Figure 1). The drastic change in functional status of skeletal muscles, which occurred during the ocean voyage, is one of the causes of the distinctive reaction of intraorganic vessels of the muscle in question at the high altitude of Antarctica. The sailing conditions lead to alteration of processes of regulation that provide for active participation of the intramuscular bloodstream in optimum adaptation of the circulatory system to the hypoxic factor.

In this regard, the previously published data [3, 7, 9] to the effect that physical and industrial factors in addition to high altitude delay processes of adaptation to high-altitude hypoxia are confirmed to some extent by the results of our investigations. In assessing the information obtained here, one should not overlook the possibility of effect of the combined set of heliophysical factors of the Antarctic continent and conditions at the Vostok Station, whichi is situated in the region of the southern geomagnetic pole [2]. The established [1] relationship between fluctuations of barometric pressure and degree of skeletal muscle capillarization in this experiment is one of the reasons for such a conclusion.

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UDC: 629.78.046:664.8.047

EFFECT OF LONG-TERM STORAGE ON SOME PARAMETERS OF FAT INGREDIENT OF FREEZE-DRIED PRODUCTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 2, Mar-Apr 86 (manuscript received 19 Dec 84) pp 69-72

[Article by A. K. Sivuk, A. G. Kasatkina, Ye. I. Strukova, V. P. Naydina and Ye. Ye. Zharkovskaya]

[English abstract from source] The effect of prolonged storage at the temperature 20±5°C and relative humidity 70-80% on the freeze-dried food products packed in a three-layer polymer was investigated. The organoleptic parameters, fat content and fat physicochemical properties were determined in the freshly prepared foods and foods stored for 6, 10 and 14 months. The fat component of cereals and vegetables was found to change during storage: the acid and peroxide numbers increased, products of secondary oxidation accumulated and nonsaturated fatty acids decreased. Among the foodstuffs examined the buckwheat cereal and mashed potatoes proved to be most stable and edible after 14 months of storage.

[Text] Dehydrated products constitute a large share (up to 65%) of the daily food allowance for crews of the Salyut station [4, 5, 9]. There are two main methods of dehydration: heat and freeze drying. The advantages of the latter are: less loss of nutrients, low weight and good reconstitution by adding water, shorter cooking time [6, 7]. At the same time, freeze-dried foods have a highly developed porous structure and large specific surface, high adsorptivity for moisture and oxygen, which could lead to overhydration of the product during storage and increase in rate of oxidative reactions [5, 12].

Storage time and freshness of fat have a considerable effect on the flavor and nutritional value of cooked foods. Some structural changes may occur in the course of obtaining fat and storing it: oxidation under the effect of air oxygen, hydrolysis under the effect of enzymes, etc. This is associated with decrease in biological value of fat, and there may be accumulation of toxic products of its oxidation. The nature and accumulation of different products of oxidative deterioration of fats depend on the combination and intensity of factors that affect fats during their processing and storage [8, 11, 14].

Our objective here was to investigate the effect of long-term storage (up to 14 months) on organoleptic properties and physicochemical parameters of fat contained in some grain and vegetable dishes dehydrated by the freeze-drying method, which were elaborated for the crews of flight vehicles.

Methods

The cooked dishes were packaged in portions of 25-50 g in an atmosphere of inert gas (nitrogen) in double cellophane and Mylar-metal RE film [2].

We tested dinner dishes that were almost cooked--buckwheat cereal, mashed potatoes and braised cabbage, which contained rendered butter as the fat ingredient, which was added to the food during preparation.

The freeze-dried foods were stored at ambient temperature of 20±5°C and relative humidity of 70-80%, i.e., under conditions that were close to those in flight vehicle cabins.

The quality of the foods was tested before storing them, as well as in the 6th, 10th and 14th months of storage. We determined organoleptic parameters (appearance, consistency, flavor, color and odor) in both dry and reconstituted forms. The physicochemical parameters included determination of total fat content in the products, presence of products of its oxidation, concentration of free fatty acids. At the present time, the most widespread methods of demonstrating fat are fat extraction with ethyl ether in Soxhlet apparatus [10], extraction with chloroform [13] and demonstration on an RLU refractometer [14]. A comparative evaluation was made of these methods in order to find the optimum one for the products under study. We also determined acid and peroxide numbers [11], levels of secondary oxidation products according to reaction with 2-thiobarbituric acid [3] and composition of fatty acids by the method of gas-liquid chromatography using a Tsvet-110 instrument.

Results and Discussion

According to a taste test, reconstitution of the foods remained good throughout the storage period. The mashed potatoes and buckwheat were given a score of 5 and braised cabbage 4.7 (on a 5-point scale) throughout the storage period.

Assay of fat content in the products under study revealed that there is the most complete extraction in the Soxhlet apparatus. With use of the refractometric method, less fat was demonstrable (by 1.5-4%) and with chloroform extraction of fat, there was 4-7% less. There was some decrease in fat content during storage, perhaps due to its partial hydrolysis. This is confirmed by the increase in free fatty acid content with extension of storage time (Figure 1). Acid number rose from 0.7580±0.0124 mg KOH (baseline level) to 1.968±0.058 mg KOH in the 14th month of storage in mashed potatoes ($P<0.01$), from 0.800±0.014 to 3.540±0.606 mg ($P<0.01$) in buckwheat and from 1.110±0.110 to 3.59±0.06 mg in the 14th month in braised cabbage ($P<0.01$). However, it should be noted that, according to the standards for acidity, the fat ingredient of all food specimens conformed to the GOST [1] both before and during the entire storage period.

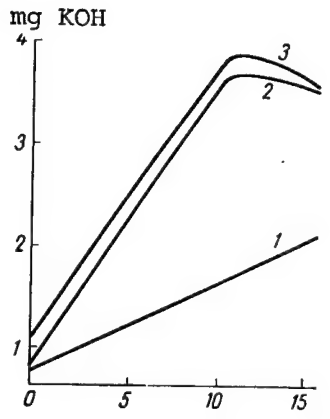

Figure 1.
Change in acid number of fat component of foods during storage

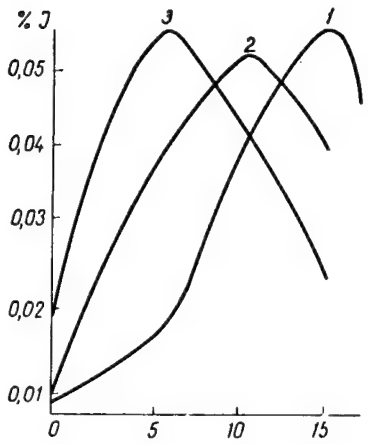

Figure 2.
Change in peroxide number of fat component of foods during storage

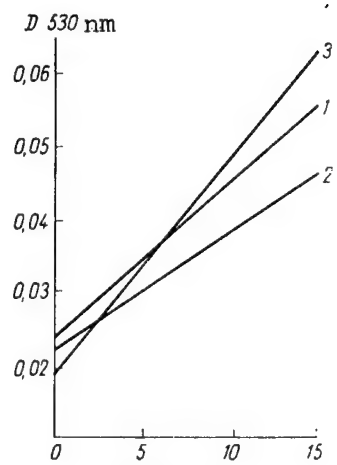

Figure 3.
Change in acidity (according to reaction with 2-TBA) of fat component during storage

Here and in Figures 2 and 3:
X-axis, month of storage
1) mashed potatoes
2) buckwheat
3) braised cabbage

The peroxide number characterizes the degree of acidity of products at the early stage of spoilage of fat. The data illustrated in Figure 2 indicate that peroxide content of mashed potatoes increases from 0.0094±0.0006 to 0.019±0.003 ($P<0.05$) in the first 6 months of storage and to 0.052±0.005 in the 14th month. Peroxide content of braised cabbage increased from 0.020±0.0002 to 0.055±0.003% iodine ($P<0.001$) in the 6th month of storage and in buckwheat it increased from 0.011±0.002 to 0.044±0.006% ($P<0.002$). A decline in peroxide content was observed in the cabbage in the 10th month and buckwheat in the 14th month.

Several studies revealed that, at the early stages of storage, the peroxide number usually increased; at the later stages it decreased due to instability of peroxides and hydroperoxides that are subject to further conversions. Being catalysts of oxidation of fat, peroxides can enter into reactions with proteins and carbohydrates, as well as decompose with formation of secondary products of oxidation of fats (aldehydes, alcohols, ketones, etc.) [8, 11, 13].

In spite of the demonstrated changes in peroxide numbers, they remained within a range that warranted consideration of the product suitable for consumption but not for further storage, according to the sanitary and hygienic standards [1].

In recent years, a method of determining rancidity of fat based on measurement of accumulation of products that react with 2-thiobarbituric acid (2-TBA) has gained wide use. These products include secondary products of oxidation of fat that are formed upon dissociation of peroxides. Determination is based on the reaction of 2-TBA with such oxidation products as malonic dialdehyde. Red products formed as a result of the reaction are quantitatively assayed by photometry at a wavelength of 532 nm. In the course of the investigation

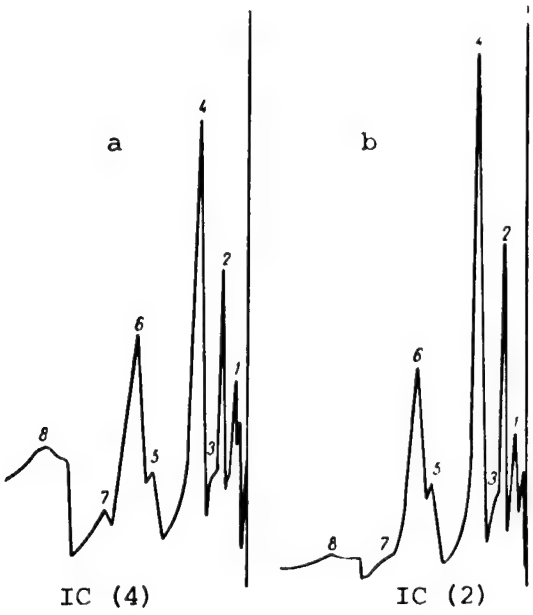

Figure 4.
Chromatograms of methyl ethers of fatty acids from buckwheat (a) and mashed potatoes (b)
1) lauric ($C_{12:0}$)
2) myristic ($C_{14:0}$)
3) pentadecanoic ($C_{15:0}$)
4) palmitic ($C_{16:0}$)
5) stearic ($C_{18:0}$)
6) oleic ($C_{18:1}$)
7) linoleic ($C_{18:2}$)
8) octadecatetraenoic ($C_{18:4}$)
IC) increase in sensitivity

it was established (Figure 3) that there was constant accumulation during storage of secondary products of oxidation of lipids that react with 2-TBA. By the 14th month of storage, optical density constituted 0.054 for mashed potatoes, 0.045 for buckwheat and 0.061 for braised cabbage. According to data in the literature, optical density of samples of butter fat in the range of 0.025-0.064 characterizes butter that is fit for storage [3].

Gas chromatographic determination of fatty acid composition of the tested types of products revealed that, among fatty acids with carbon atomic numbers of C_{12}-C_{20} (in relative percentage), saturated fatty acids constitute about 70% and unsaturated (oleic, linoleic, arachidonic) about 30%. Figure 4 illustrates typical chromatograms of the fatty acid spectrum of mashed potatoes and buckwheat. Examination of fatty acid composition of the foods revealed that there was a decrease in share of unsaturated fatty acids during storage, from 30% to 24-25% in mashed potatoes, from 34 to 14% in braised cabbage, with a corresponding increase in share of saturated fatty acids. These parameters remained virtually unchanged (30% when stored and in 14th month of storage).

Thus, the results of these investigations warrant the conclusion that the fat constituent of grain and vegetable dishes dehydrated by freeze drying underwent some changes in the course of storage for up to 14 months under our experimental conditions (increase in acid number, formation of hydroperoxides, decrease in share of unsaturated fatty acids). Buckwheat and mashed potatoes presented the lowest tendency toward oxidation. This could be related to the presence of a large amount of natural antioxidants in the original raw material. Organoleptic parameters of these dishes showed virtually no change after storage for 14 months.

On the basis of the obtained data, dishes prepared by freeze-drying consisting of buckwheat and mashed potatoes may be used in the diet of crews of flight vehicles for up to 14 months of storage under the indicated conditions.

Braised cabbage was the least stable, as indicated by the more significant accumulation of secondary oxidation products, decrease in amount of unsaturated fatty acids, worsening of organoleptic properties. This warrants the opinion that it is undesirable to use this food after 14-month storage under the indicated conditions.

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45-019:598.617.1

INVESTIGATION OF VIABILITY OF QUAIL EMBRYOS AND CHICKS WHEN EGGS ARE EXPOSED TO GAMMA RADIATION AND VIBRATION AS RELATED TO DIFFERENT TERMS OF EGG STORAGE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 2, Mar-Apr 86 (manuscript received 2 Nov 84) pp 72-77

[Article by V. F. Mishchenko and A. V. Shafirkin]

[English abstract from source] The viability of quail embryos and nestlings from the incubation eggs exposed (in) to gamma-radiation at a dose of 300 cGy and stored for 15 days or (ii) to gamma-radiation at a dose of 300 cGy and stored for 30 days or (iii) to vibration with the acute egg end oriented contrary to the vibration front and stored for 30 days did not decrease as compared to that of the controls stored for the same time period. The viability diminished if the radiation dose was increased to 600-1200 cGy or if the egg orientation during vibration was changed.

[Text] In simulating biological life-support systems (BLSS) for crews of space vehicles, there are plans to develop the component of heterotrophic organisms, one of the functions of which is to furnish the crew with food-stuffs of animal origin. Quail can be used for this purpose [10].

Development of the technology for upkeep of the birds to produce a continuous conveyer providing the crew with eggs and meat requires consideration of the distinctions of long-term spaceflights and possibility of exposure to deleterious factors at their different stages.

Deployment of a conveyer of a quail population starts with incubation of eggs, which are first submitted to a set of mechanical factors (vibration and accelerations) during powered flight. Long-term exposure to vibration accelerations could lead to structural impairment of the connections between the embryonic disk, yolk and white components of eggs and, consequently, to impaired development and decreased hatching [2].

Long-term storage of eggs before incubation and exposure to ionizing radiation are additional factors which, according to data in the literature, could lead to disruption of processes of embryogenesis and diminished viability of chicks.

Methods

For investigation of effects of ionizing radiation (Table 1), we used 920 eggs that had been stored for no more than 10 days. The 1st and 2d groups in each of three tests constituted the local control and transport control (T_1), respectively, without exposure to the main factor. Experimental groups were submitted to radiation delivered from a Start gamma unit with a ^{137}Cs source of radiation at a dose rate of 10 cGy/min in doses of 1 to 1200 cGy. Experimental batches of eggs and the transport control were transported to and from the site of irradiation in a bus. After irradiation, on the same day the eggs were placed in a laboratory incubator for further observation. We noted the relative number of developing eggs and those that "froze" at different stages of embryogenesis, determined the number of hatched chicks and their viability by the 10th day after hatching.

Table 1. Relative number of developing embryos and viable chicks after exposure of incubation eggs to different doses of γ-radiation (% of initial number of eggs; M±m)

Experiment No	Group	Absorbed dose, cGy	Number of eggs	Developing embryos in incubation periods		Viable chicks in posthatching periods	
				0 day	10th day	0 day	10th day
1	1	0	52	82,7±5,3	77,0±5,8	71,2±6,2	63,5±6,7
	2	0	53	85,0±5,5	77,5±5,8	73,7±6,2	68,0±6,5
	3	1—3	102	91,2±2,8	86,3±3,5	77,5±4,2	69,5±4,6
	4	7—12	102	85,3±3,5	79,5±4,0	69,5±4,6	63,7±4,8
2	1	0	52	82,7±5,3	75,0±6,0	50,0±7,0	30,8±6,5
	2	0	51	92,1±3,8	90,0±4,2	68,6±6,5	53,0±7,0
	3	27—50	113	92,0±2,6	80,5±3,8	50,5±4,8	37,0±4,6
	4	100—200	113	93,8±2,1	85,0±3,4	53,2±4,8	35,4±4,6
3	1	0	55	87,3±5,3	83,5±5,2	80,0±5,2	71,0±6,1
	2	0	54	92,5±3,5	83,3±5,2	70,3±6,2	57,5±6,7
	3	300	61	91,8±3,5	88,5±4,1	70,5±5,9	64,0±6,1
	4	600	55	85,5±5,2	63,5±5,6	45,5±6,7	36,4±6,5
	5	1200	57	79,0±5,4	42,0±6,5	12,3±4,4	12,3±4,4

Investigation of the effect of storage time (Table 2) was conducted using 880 quail eggs that were collected into 6 groups every 5 days. The eggs were stored in a refrigerator at a temperature of 10±1°C. After storage, they were placed in different compartments of the tray of the laboratory incubator for subsequent observation of development of embryos and hatching.

To test the effect of long-term storage of eggs combined with exposure to vibration or γ-radiation (Table 3), we used 695 eggs that had been stored for 30 days, which were delivered to the experimental base in an aircraft, and duration of flight was 3 h. To test the effect of vibration, experimental groups of eggs (with the exception of the transport control--T_2) were put in cylindrical cassettes lined on the inside with porolon [foam rubber]. The long axis of the eggs coincided with the axis of the cassette. The eggs were placed in the cassette with the pointed end to one side, and a porolon strip

was placed between adjacent eggs. The cassettes were secured on the same rigid frame, which was placed on the vibrator table, the plane (horizontal) of which was parallel or perpendicular to the axes of the cassette. In all variants of egg orientation (different experimental groups), vibration conditions were identical: buildup of frequency to 30 Hz and accelerations to 0.5 G for 18 s; increasing frequency from 30 to 50 Hz and accelerations from 0.5 to 2 G for 18 s; buildup of frequency from 50 to 2500 Hz and accelerations from 2 to 8 G 2 min 30 s; stable exposure to 2500-Hz vibration and 8-G accelerations for 3 min 48 s; reducing of vibration frequency and accelerations at the same time intervals, but in reverse order.

Table 2. Relative number of developing embryos and hatched chicks with different terms of storage of incubation eggs (% of original number of eggs; M±m)

Parameter	Preincubation storage time, days					
	1-5	6-10	11-15	16-20	21-25	26-30
Number of eggs	228	271	154	54	19	142
Developing embryos	81,2±2,6	80,1±2,5	81,2±3,2	79,6±5,5	31,6±10	31,7±3,8
Hatched chicks	70,2±3,0	68,3±3,0	72,7±3,6	64,8±6,5	26,3±10	14,1±2,9

Table 3. Relative number of developing embryos and viable quail chicks after exposure to γ-radiation or vibration of incubation eggs stored for 30 days (% of initial number of eggs; M±m)

Group	Number of eggs	Storage time, d	Additional factor	Developing embryos in incubation period		Viable chicks in posthatching period	
				0 day	10th day	0 day	10th day
1	317	1-10	Laboratory control [C]	87,1±2,0	81,1±2,0	69,1±2,5	57,5±2,8
2	138	30	Transport C	32,6±4,0	14,5±3,0	10,9±2,5	5,1±1,8
3	48	30	Vibration (lateral posit.)	31,3±6,5	6,2±3,5	2,0±2,0	2,0±2,0
4	48	30	Vibration (point down pos.)	27,0±6,4	6,2±3,5	2,0±2,0	2,0±2,0
5	48	30	Vibration (point up position)	41,5±7,0	18,7±5,5	16,6±5,3	10,3±4,3
6	48	30	300 cGy radiat.	22,5±6,0	18,3±5,6	6,2±3,5	6,2±3,5
7	48	30	500 cGy radiat.	25,0±6,2	6,9±3,6	4,2±2,9	2,1±2,1

Thus, the eggs were exposed to vibration for a total of 10 min. In the 3d group, the long axis of the eggs were parallel to the plane of the horizontal vibrator table (side position), whereas in the 4th and 5th groups, they were

perpendicular to it (with the point down and up, respectively). After exposure to the test factors and transportation, all groups of eggs were put in the laboratory incubator until chicks were hatched; chicks were under observation up to the age of 10 days.

Eggs were exposed to radiation after long-term storage using the above-described method: the 6th group received a dose of 300 cGy and the 7th, 500 cGy.

Results and Discussion

Table 1 and Figure 1 furnish data about viability of quail embryos and chicks in experimental and control groups as a function of radiation dose. As can be seen from the data in Table 1 and Figure 1, delivery of 1-300 cGy radiation failed to elicit a decline in percentage of developing embryos or hatched chicks as compared to the laboratory control (1st group). We even observed some increase (by 5-10%) in number of viable embryos and chicks, as compared to the control group. True, a stimulating effect from irradiation was observed only in the dose range of 1-3 cGy, whereas with doses of 7-300 cGy the relative number of normally developing embryos and viable chicks was the same or somewhat lower than in the transport control group. It should also be noted that in the two series of investigations, we observed an appreciable (5-20%) increase in relative number of developing embryos and particularly in number of viable chicks in the transport control group, as compared to the laboratory control (see Table 1 and Figure 2).

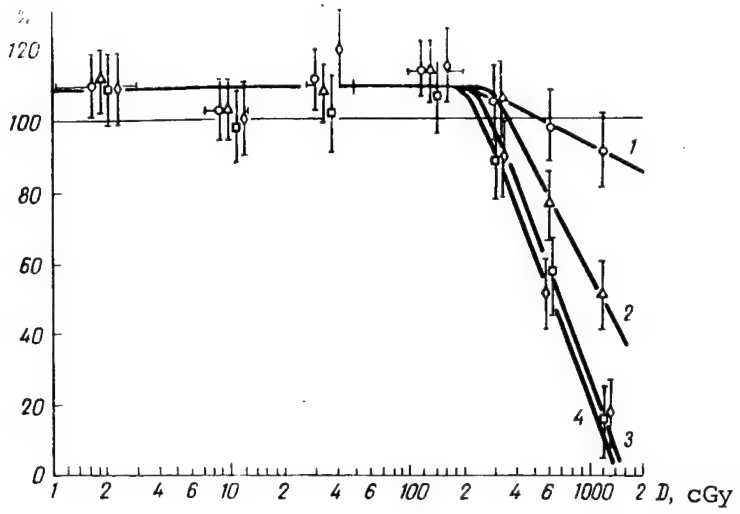

Figure 1. Change in viability of embryos and chicks as a function of dosage of γ-radiation

X-axis, absorbed dose (cGy); y-axis, relative number of viable embryos and chicks in relation to laboratory control (%)

1, 2) developing embryos at early stage of incubation and on 10th day, respectively

3, 4) hatched chicks on 0 and 10th days, respectively

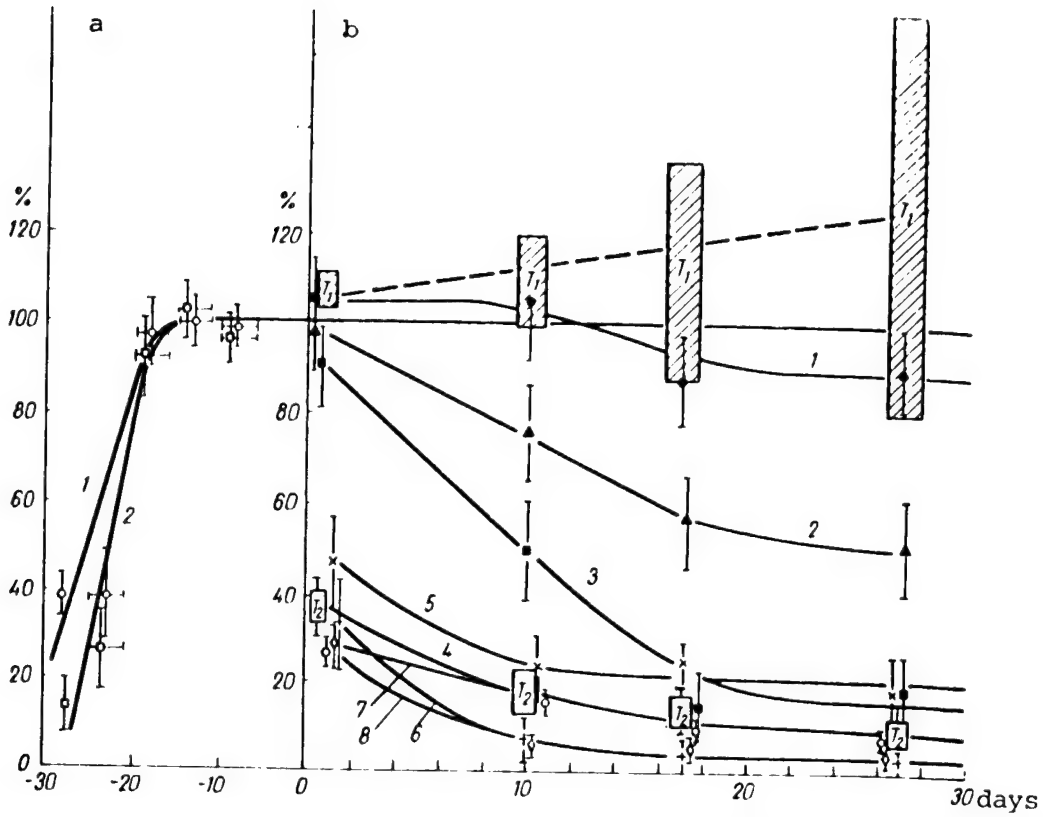

Figure 2. Change in viability of embryos and chicks under the effect of long-term storage (a), as well as radiation and combination of long-term storage with vibration or radiation (b)

X-axis: a) long-term storage of eggs before incubation
b) time from start of incubation (days)
Y-axis, relative number of viable embryos and chicks as compared to group stored for 0-5 days (a) and laboratory control (b)(%)
for a: 1) developing embryos at early stage of incubation
2) hatched chicks
for b: 1, 2, 3) radiation in doses of 300, 600 and 1200 cGy, respectively
4) transport control T_2 with 30-day storage
5) combination of 30-day storage and vibration with the pointed end down
6) same in point-up and lateral positions
7,8) combination of 30-day storage and radiation in doses of 300 and 500 cGy, respectively
Dash line and hatched bars--nature of change in viability and range of variation of values in different series of experiments in transport control group T_1

It has been repeatedly reported in the literature [4-6, 8] that low doses of radiation (3-20 cGy) have a stimulating effect on chicken eggs, and it was noted that there was acceleration of the process of embryo development,

rise in hatching percentage (by 3.5) and increase in viability of chicks in the period of up to 190 days or longer. In addition, there was an increase in egg yield of hens by 2-7% and in their live weight. At the same time, with radiation doses of 500-1000 cGy [7, 8, 14] there was substantial decrease in survival rate of embryos and viability of chicks in the postnatal period. The data obtained from experiments with quail eggs indicate that, starting with a dose of 600 cGy, there is appreciable decrease in viability of embryos and chicks, to 5/8-1/6 (see Figures 1 and 2).

Exposure to ionizing radiation occurred throughout the spaceflight. During long-term orbital flights, the dosage absorbed per year of galactic cosmic radiation and radiation from solar flares was low and did not exceeded a few tens of cGy [1, 3]. As shown by the results of investigations and data in the literature, at such levels of exposure of birds, there is no decline in their egg productivity, while exposure of incubation eggs does not lead to impairment of embryonic development or viability of chicks. We could even expect an increase by several percentage points in hatching and viability of chicks and live weight of birds.

In the case of long-term interplanetary flights beyond earth's magnetosphere, radiation from solar flares could present a substantial hazard to man and this component of the biological life-support system. For example, with shielding of 1 g/cm^2, the radiation dose from solar flares such as occurred on 23 February 1956, 10-16 July 1959 and 12-20 November 1960 would have constituted 480, 1500 and 820 cGy, respectively [3, 9]. As shown by the results of our studies and material in the literature, exposure of quail eggs to such doses leads to appreciable decline in viability of embryos and chicks. Such levels of exposure of adult birds could lead to considerable decrease in productivity and fertility, and perhaps even to their death with maximum doses [11, 13]. In view of the foregoing, when implementing such flight programs, it is desirable to place a batch of eggs and a small spare batch of birds under the radiation shield, together with the crew, for the duration of the solar flare in order to preserve productivity of the conveyer.

Tables 2, 3 and Figure 2 illustrate data on the effect of long time storage with vibrations or γ-radiation on incubation properties of eggs. From the data submitted we see that storage of eggs for up to 15 days at a stable temperature and humidity level does not affect the process of embryo development and hatching. When eggs are stored for 20 days or longer, particularly, for 25-30 days, there was a 2.5-fold decline in percentage of developing embryos and 5-fold decline in hatching (see Figure 2, curve 4).

Vibrations led to further decline of incubation properties of eggs when the long axis of the eggs was parallel to the horizontal plane of the vibrator table or perpendicular to it with the pointed end down. In the case of placing the egg axis perpendicular to the plane of the vibrator table with the pointed end up, vibration and accelerations used under the above-described conditions did not lead to decrease in viability of embryos and chicks. There was even some increase in survival rate, as compared to the transport control group (see Figure 2, curve 5). There are reports in the literature of absence of adverse effects of vibration, and even of astimulating effect on incubation properties of eggs, but without indication of their

orientation in relation to the vibration front [15]. There are also indications in the literature to the effect that, when quail eggs are stored with the pointed end up, when the yolk with embryo is in a central position in the egg, there is a substantially higher (by 3.2-14.3%) hatching rate and survival of chicks [12]. Apparently, with such position of these structures the eggs make the best use of mechanical-buffer properties of the liquid, albumen part of the egg to protect the embryo against vibrations. With other orientation of eggs, the yolk with embryo would be adjacent to the shell or the shell membrane of the egg's air chamber, as a result of which the albumen part does not protect them and they are subjected to the deleterious effect of vibrations, which could be the cause of lower viability of embryos and hatching.

Table 3 also lists data on the effects of the combination of 30-day storage and exposure to γ-radiation in doses of 300 and 500 cGy on quail eggs. As compared to the parameters for the 1st and 2d control groups (differing in storage time, and in the 2d group in presence of the factor of being transported by aircraft), as well as to the data on effects of different storage times listed in Table 2, it can be concluded that long-term storage was the principal adverse effect on embryo development, and radiation in a dosage of 300 cGy had no effect on hatching and viability of chicks, while 500 cGy lowered these two parameters to the same extent as vibrations with the egg on its side or with the pointed end down.

Thus, the results of these investigations enable us to draw conclusions and offer recommendations concerning organization and deployment of a conveyer of a quail population aboard a space vehicle as a component of the heterotrophic element of a biological life-support system, as well as development of technology for upkeep of birds and storage of eggs.

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RECLAMATION OF WATER USED FOR WASHING BY MEANS OF REVERSE OSMOSIS DURING LONG-TERM SPACEFLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 2, Mar-Apr 86 (manuscript received 15 Mar 84) pp 78-80

[Article by S. V. Polyakov, V. D. Volgin, Yu. Ye. Sinyak, Ye. D. Maksimov and V. I. Novikov]

[English abstract from source] Experiments on the purification of wash water by means of reverse osmosis membranes MGA-100 were performed. The membrane selectivity with respect to the major components (catamine AB, amine oxide and sodium chloride) was close to 100% whereas membrane permeability was not lower than 70% that of distilled water. The results of a field study in which 330 l of repeatedly used wash water were reclaimed showed that reverse osmosis can be effectively employed for that purpose.

[Text] The water to be used for personal hygiene aboard a spacecraft constitutes a significant share of the total water supply. Organization of its purification and recycling would make it possible to reduce significantly the water supply [5] taken from earth.

The water used for personal hygiene is originally distilled or tap water. After its first use, it is contaminated by washing agents, mechanical and colloid particles (mainly organic) that are washed off the cosmonaut. It also contains small amounts of other organic and inorganic substances secreted by sweat glands. Total impurities in water constitute about 1 g/ℓ. Mechanical and, in part, colloid particles can be trapped by means of various filters, in particular, microporous ones. The simplest way to remove other impurities is with sorption, using activated carbon and ion-exchange resins [1]. However, in view of the difficulty of effecting the process of sorbent reclamation under spaceflight conditions, sorbents must be used once, and this would inevitably lead to considerable outlay thereof. In addition, sorbents have a small sorbing capacity for many organic substances. In addition, wash water may also contain substances that are very poorly sorbed. All this makes it necessary to search for other methods of purification, on the basis of which it would be possible to develop a continuous water-reclamation process.

In recent years, membrane methods of separation are gaining increasing use in the national economy [2]. They are characterizied by low energy consumption, simple technological conception and high resource characteristics. The most universal and least energy-consuming of these methods is the one of reverse osmosis, the acting force of which is the gradient of hydraulic pressure through a semipermeable membrane, which plays the part of a selective barrier to impurities contained in water.

Permeate is liquid that has passed through a membrane. It contains considerably less impurities than in the original solution. The method of reverse osmosis is of maximum efficiency in processing mildly concentrated solutions, one of the representatives of which is wash water (WW).

The main constituents of WW will be washing agents, in the capacity of which a mixture of alkyldimethylbenzylammonium chloride (catamine AB) and alkyldimethylamine oxide (amine oxide) are presently used [3]. Expressly they apparently determine the choice of membranes for water treatment. Membranes with very high retention capacity for dissolved agents are needed for a high degree of water extraction in order to recover rather pure permeate.

Methods

We tested the selectivity and permeability of the most selective domestic MGA-100 membranes for aqueous solutions of catamine AB and amine oxide. Experiments were performed on a round cell with revolving magnetic mixer equipped with elastic elements in direct contact with the membrane surface, which virtually ruled out the distorting influence of concentration polarization [4]. We selected a working pressure of 5 MPa. In order to improve accuracy of evaluations, we periodically measured membrane permeability for distilled water and divided the finding by membrane permeability for the tested solutions. We tested separation of binary aqueous solutions of detergents and their mixtures. We proceeded from the fact that the ratio of catamine AB to amine oxide in WW is about 1:2. In accordance with the composition of WW, we added to the mixture sodium chloride in an amount constituting 40% of the amount of catamine AB. Maximum concentrations of tested substances were chosen on the basis of 99% yield of reclaimed water.

Results and Discussion

Tables 1 and 2 list the results of experiments on a round cell. They show that membrane permeability for the tested solutions diminished with increase in concentration. However, this decline did not exceed 30%. The membrane showed very high selective properties. The obtained data are indicative of the potentially high efficacy of reverse osmosis for treatment of WW.

The obtained data were confirmed in an experiment dealing with purification of WW obtained as a result of having subjects wash with the indicated washing agents. Water was reclaimed by passing it through a filter with mesh size of 0.5-1 μm, through a reverse osmosis apparatus with MGA-100 membrane and sorption column. The reverse osmosis apparatus of the filter-press type had 10 sections with membrane surface totaling 0.27 m^2. The apparatus operated

in a periodic mode with total recirculation of separated solution at 5 MPa. In this experiment, it was possible to wash 33 times using 30 ℓ, which was the original amount of water, 10 ℓ being the standard amount used per washing. Sorbent outlay constituted about 0.15% of the total amount of reclaimed water.

Table 1.
Permeability and selectivity of membranes as a function of concentration of detergents in water

Concentration of detergents, g/ℓ	Membrane characteristics for binary solution			
	catamine AB %		amine oxide, %	
	G	L	G	L
0,1	94	99,5	93	98,3
0,2	93	99,8	92	98,6
0,5	92	99,8	91	98,9
1,0	89	99,8	90	99,3
2,0	87	99,9	88	99,4
5,0	85	99,9	87	99,4
10,0	80	99,9	87	99,5
25,0	76	99,9	86	99,6

Note: Here and in Table 2, G is adjusted membrane permeability for solution (as related to permeability for distilled water), and L is selectivity of membrane for dissolved agent, which equals $1-c_p/c$, where c_p and c is concentration of dissolved substance in permeate and in initial solution, respectively.

Table 2.
Permeability and selectivity of membranes as a function of concentration of constituents in mixture of detergents, salt and water

Concentration of substances in mix., g/ℓ			Characteristics of membrane			
				L, %		
sodium chloride	catamine AB	amine oxide	G, %	sodium chloride	catamine AB	amine oxide
0,4	1	2	87	99,5	99,9	99,8
0,8	2	4	87	99,6	99,9	99,9
1,2	3	6	86	99,6	99,9	99,9
1,6	4	8	84	99,7	99,9	99,9
2,0	5	10	80	99,7	99,9	99,9

Table 3.
Some characteristics of water in the course of its reclamation

Monitored parameter	Purification stage			
	before filter	after filter	after reverse osmosis	after sorption
Bichromate oxidizability, mg O_2/ℓ	1332	264	45	10
Ammonia N, mg/ℓ	3,5	10	3,7	2
Chlorides, mg/ℓ	44	44	8	3
Catamine AB, "	78	18	3,5	0
Amine oxide, "	96	48	12	0
pH	7,1	7,5	7,3	7,3
Transparency, cm	0	11	30	30
Color, degrees	10	10	10	10
Odor, score	5	4	2	0

The data listed in Table 3 indicate that with 99% extraction of water the amounts of main impurities in reclaimed water do not exceed the permissible levels according to the GOST [All-Union State Standard]. According to our estimates, energy consumed for the purification process by the method of reverse osmosis will not exceed 15 W h/ℓ.

All this enables us to conclude that it is expedient to design a system on the basis of the method of reverse osmosis for purification of water that has been used for personal hygiene purposes.

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SANITARY AND MICROBIOLOGICAL ASPECTS OF CLOSED ENVIRONMENT OCCUPIED BY PEOPLE AND ANIMALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 2, Mar-Apr 86 (manuscript received 22 Jan 85) pp 80-82

[Article by V. M. Knyazev, V. I. Korolkov, A. N. Viktorov, G. O. Pozharskiy, L. N. Petrova and V. P. Gorshkov]

[English abstract from source] Men and animals (dogs) shared an enclosed environment for 30 days. The microorganisms on their skin and in the air were examined. Specific attention was given to staphylococcal pathogens that are potential causal agents of infectious diseases in enclosed bioobjects. The data obtained suggested that conditional pathogens can be exchanged between men and animals sharing an environment and clarify the mechanism(s) of their transfer. The experimental results have been used to develop prophylactic measures against diseases caused by conditional pathogens among men and animals sharing an enclosed environment.

[Text] The microflora of the habitat plays an important role among the sanitary and hygienic factors that can have an adverse effect under space-flight conditions. The results of investigations conducted aboard manned spacecraft and on the ground indicate that there is a possibility of autoinfection and cross-infection types of processes [2, 6, 10] among space-flight participants. For this reason, it is a pressing matter to conduct investigations for quantitative and qualitative evaluation of microflora isolated from people and animals during a joint stay in a pressurized environment, as well as the sanitary and microbiological characteristics of the habitat.

Methods

A 30-day investigation was conducted in a 24 m^3 pressure chamber with two communicating compartments. There were two people in one of the compartments and two dogs in special immobilization systems in the second. The tasks for experimenters included investigations of the dogs and taking constant care of them. Examination of the microflora in that environment included determination of quantitative parameters and species composition of bacterial and

fungal flora. The aspiration and sedimentation method was used to collect microflora from the air, and the conventional method of washings used in sanitary bacteriology was used to collect them from inside surfaces. The microflora from the anterior nasal mucosa was collected with dry sterile cotton sponges, while that of the mouth was collected by the washing method. We used 5% Hottinger's blood agar, mannitol and salt agar, Sabouraud agar with antibiotics as the main nutrient media. After 2-5 days of incubation at 30 and 37°C, for each group of microorganisms we counted the total number of developed colonies, isolated cultures of microorganisms and identified them. Specimens were collected from dogs from the section of their integument directly surrounding the external orifices of the nasal passages, by the impression method on sterile glass plates with Korostelev medium [4]. Strains of pathogenic staphylococci were typed by means of the international set of staphylococcal bacteriophages.

Results and Discussion

The Table lists the results of testing the microflora of the air atmosphere in the pressurized chamber compartments. According to the data listed there, there were periodic fluctuations during the investigation in microorganism content of the air in the chamber, and this is usually inherent in such conditions. We failed to demonstrate reliable differences in level of microbial contamination of the air in section No 1, where humans spent most of the time, and section No 2 with animals (total number of representatives of bacterial flora constituted 1360±280 and 1320±160 microbial cells/m^3 air, respectively). With respect to species, the bacterial flora of compartment air was represented chiefly by epidermal forms of staphylococci (over 90% of all microorganisms).

Fungal flora of the air environment of the compartments was represented mainly by mold fungi of the genus Aspergillus. The dynamics of accumulation of fungi in the air of the compartments differed in the one with animals from the one with people; in the second compartment there were more frequent periods of increase in total number of fungi. The results of examining the microflora on inside surfaces revealed that there was marked accumulation of microorganisms on the floor and walls of the chamber. The composition of microflora was analogous to the one demonstrable on the human integument.

There was also consistent increase in level of bacterial contamination of the subjects' upper respiratory tract. Total contamination of the buccal and nasal mucosa increased by 10^3-$5 \cdot 10^3$ times, as compared to the baseline period. The microflora of the mouth was represented mainly by streptococci.

Special attention was given to examination of pathogenic staphylococci on the anterior nasal mucosa, where there was more frequent localization of these microorganisms in healthy people, and they are considered the most probable pathogens of infectious diseases of people in space vehicles [1, 7]. We were impressed by the considerable size of the bacterial focus formed by pathogenic staphylococci in one subject (M-v) on the nasal mucosa. According to current conceptions, this individual can be viewed as the source of active discharge of pathogenic staphylococci into the environment [3, 8]. This is indicated by data to the effect that during periods of maximum increase in number of pathogenic staphylococci in the nose of subject M-v (from 10^4 to

10^6 microbial cells per sponge) these microorganisms were demonstrable in the air of the pressure chamber. Moreover, during periods of maximum number of phagotype 80 staphylococci, the same microorganisms were isolated from the skin of the other subject (K-v). It should be noted that we consistently isolated pathogenic staphylococci, phagotype 80, from subject M-v. Phagotype 3-A microorganisms were demonstrated in the nose of subject K-v, which did not contain staphylococci of the phagotype 80 staphylococci in the course of our study.

Bacterial contamination of the air atmosphere of the first and second compartments (quantity of microorganisms per m^3 air)

Indicator	Before study	Day of investigation									
		3	6	9	12	15	18	21	24	27	30
	First compartment										
Epidermal staphylococci	800	1060	1160	550	790	310	2860	1360	1870	1210	1440
Pathogenic "	10	-	10*	-	-	10*	-	50*	-	-	-
α-Hemolytic "	5	5	-	30	30	-	20	-	10	-	-
Corynebacteria	15	10	-	-	-	30	-	-	-	60	30
Sporogenic bacilli	90	45	20	-	20	10	-	-	10	-	-
Gram-negative bacilli	-	5	-	10	-	-	-	220	-	—	-
Gram-negative cocci	-	45	10	-	-	-	20	-	210	-	30
Total microorganisms	920	1170	1200	590	840	360	2900	1630	2100	1270	1500
	Second compartment										
Epidermal staphylococci	640	740	840	720	2280	730	1290	1020	2120	870	1320
Pathogenic "	50	-	340*	-	-	-	10*	30*	-	-	-
α-Hemolytic "	5	20	10	-	-	30	-	220	10	20	-
Corynebacteria	80	160	-	-	-	-	-	—	-	—	-
Sporogenic bacilli	30	-	-	110	20	—	-	20	70	-	10
Gram-negative bacilli	5	50	10	-	-	-	-	10	-	-	30
Gram-negative cocci	-	60	-	—	-	10	-	-	-	40	40
Total microorganisms	810	1030	1200	830	2300	770	1300	1300	2200	930	1400

Note: Asterisk refers to phagotype 80 staphylococci; dash indicates that no microorganisms were demonstrated.

The microflora of the subjects' integument during their stay in the pressure chamber was characterized by a stable level of bacterial contamination, as compared to the baseline period, and some change in species composition. There was appearance of Gram-negative bacilli, the relative number of which reached significant levels in subject M-v. At some stages of the study there was an increase in sporogenic bacilli and marked decrease in epidermal staphylococci, which are constant inhabitants of the integument of healthy man. In the course of our study, yeast-like fungi of the genus Candida and mold fungi

of the genus Aspergillus were isolated from the skin of the palm and spaces between the toes of the subjects.

In the course of the investigation, we isolated phagotype 3-A pathogenic staphylococci from the skin of dogs (from the region where electrodes were implanted). In addition, one dog presented pathogenic staphylococci of another phagotype (80). Presence of pathogenic staphylococci of the above-mentioned phagotypes warrants consideration of animals as possible recipients and sources of pathogens in the environment. There can be interchange of microorganisms not only in the case of direct contact between people and animals, but through the air environment. Our findings are indicative of a need to elaborate measures for prevention of diseases induced by conditionally pathogenic microorganisms in people and animals when both share the same closed environment. Self-contained life-support systems for humans and animals could be one of the effective protective steps, as has also been indicated by other researchers [5, 9].

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EFFECT OF HYDROCORTISONE ON OSTEOGENIC FUNCTION OF MOUSE BONE MARROW

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by T. Ye. Burkovskaya]

[English abstract from source] Bone marrow cells were implanted into the capsule of the kidney of mice which were then given intraperitoneal injections of hydrocortisone in the dose of 5 mg per animal. The drug influenced different stages of bone histogenesis in a different manner. The stage of onset of bone formation proved to be most sensitive, whereas the earlier and later stages were less sensitive to hydrocortisone. It is concluded that the target cells for hydrocortisone are osteoblasts at the stage of active synthesis of bone proteins rather than cells-precursors of osteogenesis.

[Text] Sufficient facts have been accumulated to date to indicate that osteoporosis develops in weightlessness and under hypokinetic conditions in both man and animals [1, 4, 14]. However, the mechanism of loss of bone mass under these conditions has not been adequately investigated. It is believed that the lack of static skeletal function is the prime factor causing osteoporosis in weightlessness and model experiments. However, this does not rule out the influence of other factors, primarily stress-producing ones, which is particularly inherent in laboratory animals [2, 10]. To what extent could corticosteroids make a contribution to development of osteoporosis? To answer this question, an adequate model must be selected that would permit reproduction of bone histogenesis in an adult organism. Heterotopic transplantation of bone marrow fragments under the renal capsule is one such model [3]. In this case, bone tissue of donor origin is formed at the implantation site from determined precursor cells, and subsequently recipient bone marrow develops in it [3], i.e., there is formation of a distinctive osseous organ, the structure of which does not differ from bone tissue of the skeleton, and at the same time, unlike the latter, it is free of the influence of dynamic and static loads. Thus, this model rules out the load factor and enables us to assess the contribution of other factors that may be present in ground-based model experiments and in weightlessness.

We investigated here, in particular, the effect of hydrocortisone (HC) on osteogenetic function of mouse bone marrow by the method of heterotopic transplantation, which enabled us to assess, to some extent, the relevance of the stress factor to impairment of this function.

Methods

Experiments were conducted on male CBA and hybrid F_1(CBA×C57BL) mice, in which half the bone marrow contained in the femur of a syngeneic donor was implanted under the renal capsule. Bone marrow was flushed with a syringe into medium 199 under refrigeration (4°C). Recipients were operated under nembutal anesthesia with addition of ether.

In order to demonstrate the differentiated effect of HC on osteogenic precursor cells or mature osteoblasts, we conducted 2 variants of experiments: 1) HC given once to donors 1, 3 and 5 days before extraction of bone marrow and 2) HC given once to recipients on the 1st, 3d, 5th, 10th and 14th days after transplanting cells. In addition, we performed an experiment on 7 mice, to which the hormone injection was given 6 times every 3-4 days, starting on the 3d day after implantation of bone marrow. HC (injectable microcrystals) was injected intraperitoneally in a dosage of 5 mg/mouse.

Mice used in all of the experiments were decapitated by a bloodless method on the 22d-23d day after cell implantation in order to examine ectopic bone. We evaluated the general appearance of transplants, weighed them and, for pharmacological evaluation of effect of HC, we extracted and weighed the thymus and spleen. Smears of bone marrow taken from the ectopic bone were stained according to Romanovskiy, and we counted the percentage of main hemopoietic precursors. The digital data were assessed using Student's t criterion.

Results and Discussion

Single injection of HC to donors 1, 3 and 5 days before extraction of cells did not have an appreciable effect on osteogenetic function of bone marrow (Table 1). However, in this case the weight of ectopic bone that grew under the renal capsule was somewhat lower on the average than in animals in which bone marrow from intact mice was implanted, but the differences were statistically unreliable.

Single injections of HC to recipients on the first 3 days after transplantation of intact bone marrow (see Table 1) also had no appreciable effect on development of ectopic bone. According to the data of A. Ya. Fridenshteyn et al. [3], at this stage a significant part of the hemopoietic cells in the grafts present signs of degeneration, and bone fragments carried into the grafts become necrotic. Sites of new osteogenesis appear only on the 4th-6th day. They consist of groups of osteoblasts surrounded by basic substance in the form of fine osseous trabeculae. Administration of HC in this period (5th-10th day after implantation) did not block osteogenesis entirely, and foci of osteogenesis were demonstrable in all animals; however, its inhibitory effect on this phase of osteogenesis was apparent. The weight of newly formed bone was half the value of control animals. Most often, several small bones

Table 1.
Heterotopic osteogenesis (22d-23d day after implantation of cells under renal capsule)

Variant of experiment	Day of giving HC	Number of experim.	Number of mice	Weight of bone under renal capsule, mg (M±m)
Control	—	14	46	1,05±0,16
HC to donor	1	2	15	0,81±0,13
	3	2	12	0,89±0,67
	5	2	14	0,81±0,15
HC to recipient	1	3	19	1,29±0,14
	3	3	16	0,80±0,22
	5	2	18	0,56±0,14*
	10	2	11	0,46±0,08**
	14	2	13	0,77±0,08

*P<0.02, as compared to control.
**P<0.001, as compared to control.

with sharp edgs were formed, which sometimes grew together in a very fine lacy pattern.

Two-week old ectopic bone, which developed in intact animals that were not given HC, consists of a well-formed medullary organ covered with a lacy bone sheath on the side of the renal capsule and filled with actively proliferative bone marrow. According to the results of an additional experiment performed on 9 animals, which were decapitated on the 14th day after implantation of bone marrow, ectopic bone weight constituted a mean of 0.49±0.14 mg. Injection of HC on the 14th day reduced somewhat the rate of development of bone and marrow. Average bone weight by the end of the experiment, in this case, constituted 0.77 mg, versus 1.05 mg in the intact control (see Table 1).

In the case of a constantly elevated HC level (6 injections in 23 days), there was virtually complete suppression of ectopic osteogenesis. Tiny bones, weighing less than 0.1 mg, showing no signs of development of bone marrow in them, were formed in only 30% of the cases.

It is known that glucocorticoid-related osteoporosis usually develops with chronic intake of products [5, 12, 15], and it is attributable to two simultaneous processes: direct depression of osteogenesis and accelerated resorption of bones [15]. Slower osteogenesis is usually attributed to direct inhibition of osteogenetic function. The model of ectopic bone that we used emphasizes attention on the osteogenetic process, whereas use of single injections of HC at different stages of osteogenesis enabled us to demonstrate the sensitivity of different stages of histogenesis to this hormone. In addition, the advantage of the model use enables us to trace the effect of HC on osteogenic precursor cells which, in turn, broadens our conception of the mechanism of HC action.

The lack of effect with single injection of HC to bone marrow donors, as well as on the 1st day after implantation of cells, indicates that osteogenic precursor cells are relatively resistant to HC: their osteogenic capacity is retained to some extent or other in all variants of the experiment. The inhibitory effect of HC is demonstrable at the early stage of bone formation (5th-10th days). This period is characterized by active proliferation of osteogenic cells, which furnishes a sufficient supply of osteoblasts that start to synthesize collagen. Evidently, there is expression here of the universal property of glucocorticoids: depression of proliferative activity of cells which, along with depression of biosynthesis of bone proteins, inhibits

build-up of bone. Apparently, the combination of these two processes is the reason for maximum sensitivity to HC at the starting phase of bone formation.

Along with depression of osteogenesis, glucocorticoids stimulate resorption of skeletal bone tissue both by direct stimulation of osteoclast activity [17] and indirectly, by changing the levels of parathyroid hormone [7, 11] and calcitonin [13], increasing sensitivity to active metabolites of vitamin D_3 [8, 16] and decreasing thymus function [6].

The phenomenon of involution of the thymus-lymphoid system with administration of HC is well-known. Thymectomy on rats elicited drastic reduction of the epiphyseal growth plate and its zones [6]. The opinion is held that involution of the thymus causes reduction in the population of monocytes, and thereby depresses osteoclast formation, which impairs processes of reshaping bone [6].

Under our experimental conditions, weight of the spleen and thymus was not entirely restored after giving HC to recipients. In experimental animals, the weight of these organs with administration of HC was statistically lower at all tested times after cell implantation than in controls ($P<0.001$). Minimal values for these parameters were recorded in the case where HC was given on the 10th-14th day after transplantation of bone marrow, which they constituted 42.3 and 13.3% of control weight of the spleen and thymus, respectively. At expressly this period we observed minimal bone weight. For this reason, it can be assumed tat there is a cause and effect relationship between atrophy of the thymus and lymphatic system, on the one hand, and inhibited development of ectopic bone, on the other. However, this question is still open.

Table 2. Cytological composition of bone marrow in ectopic bone (main elements of hemopoiesis, %, M±m)

Variant of experiment	Day of giving HC	Erythroid elements	Granulocytes	Lymphocytes
Control	-	26,05±1,60	35,65±2,34	34,15±2,83
HC to donor	1	26,35±1,78	37,36±2,34	27,70±1,72
	3	21,25±6,74	42,50±4,21	33,50±2,80
	5	25,50±2,65	41,87±4,77	26,93±6,09
HC to recipient	1	29,93±1,31	41,67±1,93	24,40±2,62*
	10	18,64±1,38**	51,14±1,79**	25,64±1,63**
	14	32,55±2,14*	40,66±2,26	23,00±2,50**

*P<0.05, as compared to control.
**P<0.01, as compared to control.

Analysis of medullary hemopoiesis in ectopic bone revealed depression of lymphopoiesis. The percentage of lymphoid cells dropped reliably after HC (Table 2). However, this decline (to 67% of the control) was less marked than involution of the thymus. Apparently this is attributable to the fact that skeletal bone marrow, like that of ectopic bone, is populated mainly by B lymphocytes which are, as we know, less sensitive to glucocorticoids than T lymphocytes [9].

The changes in number of erythroid and granulocytic cells demonstrated under the effect of HC on the 10th and 14th days of development of ectopic bone are episodic, so that it is difficult to interpret them at the present time.

Thus, the results of this investigation lead us to conclude that even acute one-time elevation of corticosteroid level is associated with inhibition of bone histogenesis which, in turn, leads to reduction in rate of build-up of bone. Such a situation can arise both in weightlessness and under hypokinetic conditions, since both factors elicit a stress reaction. Apparently, elevation of corticosteroid level contributes to development of osteoporosis as a result of inhibition of de novo osteogenesis. The data of E. R. Morey [14] confirm this; she observed arrested bone growth in rats on the 11th day of a space-flight. It is difficult to determine for the time being whether HC has a direct or indirect effect on bone histogenesis. It appears that both routes of action of this hormone on the process of osteogenesis are possible, since this process is associated with impairment of hormonal balance and changes in other tissue systems.

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MATHEMATICAL MODEL OF CUPULOENDOLYMPHATIC SYSTEM WITH DIFFERENT CUPULA AND ENDOLYMPH DENSITIES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by A. V. Kondrachuk and S. P. Sirenko]

[English abstract from source] This paper presents a mathematical model of time-course variations of the cupulo-endolymphatic system which can be described by the Steinhauzen phenomenological equation for the case of a unidimensional toroid, assuming that the densities of the cupula and endolymph are identical. If the densities are different, the time-course variations of the cupuloendolymphatic system may aggravate and manifest at the powered stages of space flight.

[Text] In recent years, there has been a sharp increase of interest in research in the field of biophysics of the vestibular system (VS) in connection with the need to develop and use new transport equipment, first of all in space and in the air [3]. The purpose of such research is to determine the causes and mechanisms of onset of motion sickness under such conditions. One of its causes could be impaired function of the semicircular canals as a hydromechanical sensor of accelerations and velocities under conditions of period exposure to dynamic factors and altered gravity.

The system of the three semicircular canals consists of a membranous sheath with a complicated shape (Figure 1). Each canal has a shape that is close to a torus. The canal planes are approximately perpendicular to one another. The two vertical canals merge and form a common pedicle. Each canal has a dilatation--the ampulla. In the ampulla there is a crista, which is a receptor structure consisting of pillar and sensory cells (Figure 2). There is a gelatinous cupula covering the ampulla which presents a solid obstacle to fluid (endolymph), which fills the entire membranous sheath. When the head turns, the endolymph is inertially displaced and moves the cupula over the crista. This is associated with irritation (deformation) of sensory cell hairs, from which information about movement of the cupula is transmitted to the central nervous system.

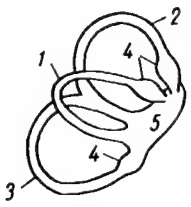

Figure 1.
System of semicircular canals
1) horizontal semicircular canal
2) anterior " "
3) posterior " "
4) ampullae of canals
5) utriculus

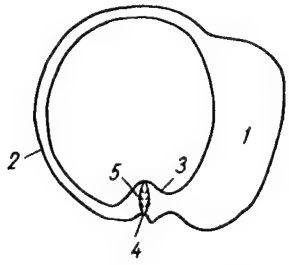

Figure 2.
Semicircular canal
1) utriculus
2) canal
3) ampulla
4) crista
5) cupula

Steinhausen's model [15] was the first mathematical model of cupula movement in the semicircular canal; in it the behavior of the cupuloendolymphatic system (CES) was described by an equation for a damped oscillator:

$$\ddot{\zeta} = -2h\dot{\zeta} - \omega_0^2\zeta - f(t). \qquad (1)$$

It was assumed that the magnitude of viscous friction is determined by the viscous friction of endolymph on the canal surface, while the elasticity coefficient is determined by the resilient attachment of the cupula on the crista. There is a considerable number of works [1, 3, 5] dealing with analysis of this equation as applied to various exogenous factors, and they have shown that phenomenological equation (1) reflects the basic features of CES dynamics.

Explanation of the nature of the extremely low threshold of CES sensitivity is one of the unsolved problems in VS biophysics. For this reason, much attention has been devoted in recent times to investigation of the effect of shape and structure of the cupula, nature of cupular movement over the crista on dynamic behavior of the CES [6, 7, 9, 11, 12].

There are some experimental data that are not described by equation (1), which lead us to assume that CES dynamics are more complex [2]. The differences between experimental results and those predicted by equation (1) were attributed to the distinctions of information processing in the cupula-nerve fiber element [8]. However, several of them could have been due to some of the physical characteristics of CES that were not taken into consideration in the model of Steinhasen [15], in particular, a difference in density of the cupula and endolymph.

We have examined the following model of the cupula-endolymph hydromechanical system: a) semicircular canal-isolated torus with solid walls entirely filled with homogeneous viscous fluid (endolymph) with density ρ_1; b) the cross-section of the canal is entirely covered by a piston (cupula) with density ρ_2 that is attached to the wall of the torus. Consideration of viscosity in a

system with such geometry leads to great mathematical difficulties. However, it is not difficult to show that, in the absence of a piston, the force of friction of fluid against the wall of a torus is, with good approximation, proportionate to velocity of the fluid. The same follows from the phenomenological description of movement of the cupula. For this reason, we shall consider the fluid to be ideal, and we shall add the term with linear viscous friction to the equation for piston movement. It is logical to assume that the force of elasticity is a linear function of displacement with low deviations of the cupula.

Let us assume that the piston has one degree of freedom $\xi(t)$, it is an absolutely solid body and overlaps entirely the torus section for fluid. The fluid and piston are in a field submitted to the force of gravity.

Let us analyze the behavior of such a system when it rotates at angular velocity $\vec{\omega}$ in relation to the specified axis situated at distance λ from the center of the torus.

We derive the equation of movement using Hamilton's variation principle:

$$\delta \int_{t_1}^{t_2} T\,dt + \int_{t_1}^{t_2} \delta A\,dt = 0, \tag{2}$$

where T is kinetic energy of the system, variation of which equals

$$\delta T = -\sum_{i=1}^{2} \iiint_{V_i} \rho_i \left\{ \dot{\vec{v}}_i + [\dot{\vec{\omega}} \times (\vec{R}_i + \vec{\lambda})] + \right.$$
$$\left. + 2[\vec{\omega} \times \vec{v}_i] + \vec{\omega} \times [\vec{\omega} \times (\vec{R}_i + \vec{\lambda})] \right\} \delta \vec{R}_i\,dV_i, \tag{3}$$

where $\vec{V}_1$, $\vec{v}_2$ are velocities of fluid and piston; $\vec{R}_1$, $\vec{R}_2$ are vector radii drawn in elementary volumes of fluid and piston from the center of the torus; A is work of forces acting on the system, variation of which is written down in the following form:

$$\delta A = \delta A_{fr} + \delta A_{el} + \sum_{i=1}^{2} \iiint_{V_i} \rho_i \vec{g}' \delta \vec{R}_i\,dV_i -$$
$$- \iiint_{V_1} \delta \vec{R}_1 \operatorname{grad} p\,dV_1 + \oint\!\!\oint_{S_2} \delta \vec{R}_2 \vec{n} p\,dS_2; \tag{4}$$

A_{fr}, A_{el} are work of forces of viscous friction and elasticity, $\vec{g}'$ is acceleration of gravity field in the system of torus coordinates, p is

pressure, $\vec{n}$ is the normal to the external surface of the piston, the term $\iiint_{V_1} \delta\vec{R}_1 \operatorname{grad} p dV_1$ was obtained from the expression $\iiint_{V_1} div(p\delta\vec{R}_1) dV_1$ [4], with consideration of incompressibility of fluid; $div\ \vec{v}_1 = 0$.

The link between accelerations of gravity filed in the mobile system of coordinates of the torus and immobile inertial system, which begins on the axis of rotation, is expressed as follows:

$$g_1' = \beta_{11}g_1 + \beta_{21}g_2 + \beta_{31}g_3,$$
$$g_2' = \beta_{12}g_1 + \beta_{22}g_2 + \beta_{32}g_3,$$
$$g_3' = \beta_{13}g_1 + \beta_{23}g_2 + \beta_{33}g_3,$$

where β_{ij} are direction cosines.

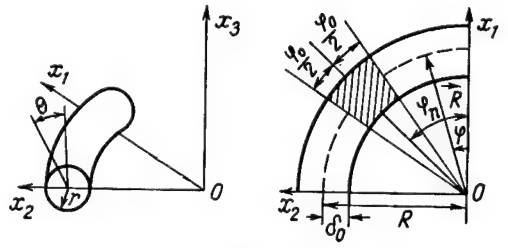

Figure 3.
System of toroidal coordinates and symbols used to derive equations for CES

For a torus (Figure 3):

$$\vec{R}_1 = (R + r\sin\theta)\cos\vec{\varphi}_i +$$
$$+ (R + r\sin\theta)\sin\vec{\varphi}_j + r\cos\theta\vec{k},$$
$$\vec{R}_2 = (R + r\sin\theta)\cos(\varphi + \varphi_n + \zeta)\vec{i} +$$
$$+ (R + r\sin\theta)\sin(\varphi + \varphi_n + \zeta)\vec{j} + r\cos\theta\vec{k}.$$

According to the experimental results, δ_0 is considerably smaller than $R(\delta_0/R \approx \frac{1}{20} \div \frac{1}{10})$. In zero approximation for δ_0/R, fluid has one degree of freedom and because of the incompressiblity of liquid and piston their movement is described by one coordinate. Consequently, with consideration of this approximation, variations $\delta\vec{R}_1$ and $\delta\vec{R}_2$ will have the following appearance:

$$\delta\vec{R}_1 = [-\sin(\varphi + \zeta)\vec{i} + \cos(\varphi + \zeta)\vec{j}]\, R\delta\zeta,$$
$$\delta\vec{R}_2 = [-\sin(\varphi + \varphi_n + \zeta)\vec{i} +$$
$$+ \cos(\varphi + \varphi_n + \zeta)\vec{j}]\, R\delta\zeta, \qquad (5)$$

and the pressure function depends only on variables t and $\varphi + \zeta$.

Let us insert expression (5) in equations (3) and (4) and then insert the obtained equations in equation (2). After integration for volume of liquid and piston and equating to zero the expression with $\delta\xi$, we arrive at the equation for movement of the system in question:

$$\begin{aligned}\ddot{\zeta} = &-2h\dot{\zeta} - \omega_0^2\zeta - \dot{\omega}_3 - \Delta m_1 \times \\ &\times\left[2\omega_1\omega_2 \cos 2\left(\varphi_n + \zeta\right) + \right. \\ &\left. + \left(\omega_2^2 - \omega_1^2\right) \sin 2\left(\varphi_n - \zeta\right)\right] - \\ &- \Delta m \left\{\sin\left(\varphi_n + \zeta\right)\left[\lambda_1\left(\omega_2^2 + \omega_3^2\right) + \right.\right. \\ &\left. + \lambda_2\left(\dot{\omega}_3 - \omega_2\omega_1\right) - \lambda_3\left(\dot{\omega}_2 + \omega_3\omega_1\right) + g_1'\right] - \\ &- \cos\left(\varphi_n + \zeta\right)\left[\lambda_3\left(\dot{\omega}_1 - \omega_2\omega_3\right) + \right. \\ &\left.\left. + \lambda_2\left(\omega_3^2 + \omega_1^2\right) - \lambda_1\left(\omega_1\omega_2 + \omega_3\right) + g_2\right]\right\}. \qquad (6)\end{aligned}$$

where

$$\Delta m = \frac{2\left(\rho_2 - \rho_1\right)\pi\delta_0^2 \sin\varphi_0/2}{m + M},$$

$$\Delta m_1 = \frac{\left(\rho_2 - \rho_1\right)\pi\delta_0^2 R \sin\varphi_0}{2\left(m + M\right)},$$

$$2h = \frac{\gamma}{m + M}, \quad \omega_0^2 = \frac{k}{m + M},$$

(m is piston mass and M is fluid mass).

In deriving this equation, we took into consideration the fact that, by virtue of Newton's third law, terms $\iiint_{V_1} \operatorname{grad} p dV_1$ and $\oint_{\sigma_2} \pi \rho d\sigma_2$ are mutually cancelled out, moment of friction force Q_{fr} equals $-\gamma R^2\zeta$ and moment of elasticity force Q_{el} equals $-kR^2\zeta$.

With $\rho_1 = \rho_2$, the obtained equation (6) changes into equation (1). If, however, $\rho_1 \neq \rho_2$, piston movement starts to depend on rotation parameters $\vec{\lambda}$ and $\vec{\omega}$.

In the general case, equation of movement (6) has a rather complicated appearance with $\rho_1 \neq \rho_2$. For this reason, we shall discuss some special instances of movement on the assumption that $\zeta \ll 1$ and then considering equations that are linear for ζ. This approximation is attributable to the low value of coefficient ω_0^2 as compared to $2h(\omega_0^2/2h \approx 0.05$ [14]) and values for parameters of exogenous factors used in CES studies. According to movement equation (6), in the case of linear approximation, the coefficient with ζ--coefficient of system elasticity--depends on parameters of exogenous factors. However, the values used for the exogenous factor parameters do not change appreciably the coefficient of system elasticity, and for this reason it remains in a damped state, which leads to absence in direct expansion of secular terms and terms with low denominators with asymptotic solution of equation (6).

Let us define orientation of the axis of rotation and vector of gravity in relation to the torus plane with condition A:

$$\lambda = (0, -\lambda, 0), \quad \vec{g} = (-g, 0, 0), \quad \vec{\omega} = (\omega, 0, 0)$$

(Figure 4), then equation of movement (6) will acquire the following appearance:

$$\ddot{\zeta} = -2h\dot{\zeta} - a\zeta + b, \tag{7}$$

where

$$a = \omega_0^2 - \omega^2 \left(\alpha \sin \varphi_n + 2\Delta m_1 \cos 2\varphi_n\right) - \\ - \Delta g \cos \varphi_n,$$

$$b = \omega^2 (\sin 2\varphi_n \, \Delta m_1 - \alpha \cos \varphi_n) + \Delta g \sin \varphi_n,$$

$$\Delta g = \Delta m g, \quad \alpha = \Delta m \lambda.$$

Let $\omega = \text{const}$, $\zeta|_{t=0} = \zeta_0, \dot{\zeta}|_{t=0} = 0$

(case A.1). With the chosen orientation of the system in relation to vector g, in the case of $\varphi_n = j\pi (j = 0, 1, \ldots)$, due to the difference in densities the cupula shifts under the effect of gravity; at the start of rotation there is no pulse of inertial forces upon the CES, rather it is caused by change in elastic parameter of the system.

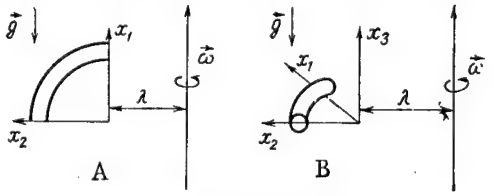

Figure 4.
Orientation of axis of rotation and vector of gravity in relation to plane of torus. Conditions A and B; see text

The solution of equation (7) will have the following appearance:

$$\zeta = C_1 e^{k_1 t} + C_2 e^{k_2 t} + \frac{b}{a}, \tag{8}$$

where

$$C_1 = -\frac{a\zeta_0 - b}{a(k_1 - k_2)} k_2,$$

$$C_2 = \frac{a\zeta_0 - b}{a(k_1 - k_2)} k_1, \quad k_{1,2} = -h \pm \sqrt{h^2 - a}.$$

Thus, with $t \to \infty$ the cupula will be displaced by b/a.

Let $\omega = -A\cos\gamma t$, $\varphi_n = 0$ (case A.2). In this case, we arrive at an equation with variable coefficients:

$$\zeta'' = -2\mu\zeta' - \zeta[\delta - \varepsilon \cos \gamma\tau] - D - D\cos\gamma\tau, \tag{9}$$

$$\tau = \omega_0 t, \quad \mu = \frac{h}{\omega_0},$$

$$\delta = \frac{\omega_0^2 - \Delta g - \Delta m_1 A^2}{\omega_0^2},$$

$$\varepsilon = \frac{\Delta m_1 A^2}{\omega_0^2}, \quad D = \frac{\alpha A^2}{2\omega_0^2}, \quad \gamma = \frac{2\nu}{\omega_0}.$$

Assuming that $\varepsilon \ll 1$, we search for a solution in the following form:

$$\zeta = \zeta^0 + \varepsilon\zeta_1 + \varepsilon^2\zeta_2 + \cdots \tag{10}$$

Inserting (10) in equation (9), after conversions with $t \to \infty$ we shall obtain:

$$\zeta = a_1\left(1 + \frac{\varepsilon}{\delta}\right)\cos(\gamma\tau + \beta) + \varepsilon a_1 a_2 \cos(2\gamma\tau + \beta + \beta_1) + \frac{\varepsilon}{2\delta} \times \times a_1 \cos\beta - \frac{D}{\delta} + o(\varepsilon^2), \tag{11}$$

where

$$a_1 = D\left[(\delta - \gamma^2)^2 + (2\mu\gamma)^2\right]^{-1/2},$$

$$a_2 = \frac{1}{2}\left[(\delta - (2\gamma)^2)^2 + (4\mu\gamma)^2\right]^{-1/2},$$

$$\operatorname{tg}\beta = \frac{2\mu\gamma}{\gamma^2 - \delta}, \quad \operatorname{tg}\beta_1 = \frac{4\mu\gamma}{(2\gamma)^2 - \delta}.$$

Let us note that, due to the fact that $2\mu > \sqrt{\delta}$, the obtained direct expansion is uniformly suitable.

According to (11), consideration of terms $\sim\varepsilon$ leads to appearance of additional multiple frequencies in oscillations of the cupula and a shift of its equilibrium position.

Let $\varphi_n = \Pi/2$, $\omega = -A\cos\nu t$ (case A.3).

Then:

$$\zeta'' = -2\mu\zeta' - \zeta\left[W - \sigma\cos\gamma\tau\right] + d,$$

where

$$W = \frac{\omega_0^2 - {}^1/_2 A^2(\alpha - 2\Lambda m_1)}{\omega_0^2}, \tag{12}$$

$$\sigma = \frac{A^2(\alpha - 2\Lambda m_1)}{2\omega_0^2}, \quad d = \frac{\Delta g}{\omega_0^2}.$$

With $\sigma \ll 1$ the solution of equation (12) with $t \to \infty$, will have the following appearance with margin of error to first-order terms for σ:

$$\zeta = \frac{d}{W} + \sigma a\cos(\gamma\tau + \beta) + o(\sigma^2), \tag{13}$$

where

$$a = \frac{d}{W}\left[(W - \gamma^2)^2 + (2\mu\gamma)^2\right]^{-1/2},$$

$$\operatorname{tg}\beta = \frac{2\mu\gamma}{\gamma^2 - W}.$$

Consequently, oscillations of the cupula in this case occur in relation to the shifted position, which arises as a result of the effect of gravity on the CES.

Let us define orientation of the axis of rotation and vector of gravity in relation to the torus plane with condition B:

$$\lambda = (0, -\lambda, 0), \quad g = (0, 0, -g), \quad \vec{\omega} = (0, 0, \omega)$$

(Figure 4B)

Then from (6) we have:

$$\ddot{\zeta} = -2h\dot{\zeta} - \zeta\left[\omega_0^2 - \alpha\left(\dot{\omega}\cos\varphi_n + \omega^2\sin\varphi_n\right)\right] - \dot{\omega} - \alpha\left(\omega^2\cos\varphi_n - \dot{\omega}\sin\varphi_n\right). \tag{14}$$

Within the framework of the model under discussion, with such orientation of the system, dynamics of the cupula are unrelated to $\vec{g}$.

$$\text{Let } \omega = \text{const}, \ \zeta|_{t=0} = 0, \ \dot{\zeta}|_{t=0} = \dot{\zeta}_0$$

(case B.1), under this condition a pulse of inertial forces arises at the first point in time.

The solution of (14) can be written down as follows:

$$\zeta = C_1 e^{k_1 t} + C_2 e^{k_2 t} - \frac{D}{Q}, \tag{15}$$

where

$$C_1 = \frac{D}{Q} - \frac{Q\dot{\zeta}_0 - k_1 D}{Q(k_2 - k_1)},$$

$$C_2 = \frac{Q\dot{\zeta}_0 - k_1 D}{Q(k_2 - k_1)}, \quad D = \alpha\omega^2\cos\varphi_n,$$

$$Q = \omega_0^2 - \alpha\omega^2\sin\varphi_n, \quad k_{1,2} = -h \pm \sqrt{h^2 - Q}.$$

Analogously to case A.1, with $t \to \infty$ $\zeta \to -\frac{D}{Q}$.

Let $\omega = -A\cos\nu t$, $\varphi_n = 0$ (case B.2). Then equation (14) will assume the following appearance:

$$\zeta'' = -2\mu\zeta' - \zeta[1 - \varepsilon\sin\gamma\tau] - \varkappa\sin\gamma\tau - \varepsilon\beta(1 + \cos 2\gamma\tau), \tag{16}$$

where

$$\tau = \omega_0 t, \quad \gamma = \frac{\nu}{\omega_0},$$

$$\varkappa = \frac{A\nu}{\omega_0^2}, \quad \varepsilon = \frac{\alpha A\nu}{\omega_0^2}, \quad \beta = \frac{A}{2\nu}, \quad \mu = \frac{h}{\omega_0}.$$

With $\varepsilon \ll 1$ and $t \to \infty$, we shall obtain a solution to the equation with a margin of errors to first-order term for ε:

$$\zeta = a_1 \sin \gamma\tau + a_2 \cos \gamma\tau + \varepsilon L_1 \sin 2\gamma\tau + \\ + \varepsilon L_2 \cdot \cos 2\gamma\tau + \varepsilon \frac{(a_1\gamma^2 - \varkappa)}{2\gamma^2} + o(\varepsilon^2),$$

where $$a_1 = \frac{\varkappa(\gamma^2 - 1)}{(1-\gamma^2)^2 + 4\mu^2\gamma^2},$$

$$a_2 = \frac{2\varkappa\mu\gamma}{(1-\gamma^2)^2 + 4\mu^2\gamma^2}, \qquad (17)$$

$$L_1 = -\frac{1}{2} \frac{Q_2(1-4\gamma^2) - 4(a_1 + \varkappa/\gamma^2)\mu\gamma}{(1-4\gamma^2)^2 + (4\mu\gamma)^2},$$

$$L_2 = -\frac{1}{2} \frac{4\mu\gamma a_2 + (a_1 + \varkappa/\gamma^2)(1-4\gamma^2)}{(1-4\gamma^2)^2 + (4\mu\gamma)^2}.$$

Just as in the case of A.2, oscillatory movement of the cupula occurs near the shifted position, and it is represented by the sum of oscillations at multiple frequencies.

The most elementary special instances of movement we have discussed, which are given by a combination of parameters $\vec{\lambda}$, $\vec{\varphi}_{\gamma_i}$ and $\vec{\omega}$, indicate that behavior of the cupula differs appreciably from the one predicted with equation (1) when there is a difference in density of the cupula and endolymph.

Using equation of CES movement (6), let us estimate the difference between density of the cupula and endolymph. Let us assume that $\omega_0^2 \sim 10\ s^{-2}$, $(m + M) \sim 10^{-2}$ g, $V_2 \sim 10^{-3}$ cm [14]. According to equation (6), in case A (gravity vector in plane of torus) the cupula is deviated by $|\zeta| = \Delta g/\omega_0^2 \sim 10^2 |\Delta\rho|$ rad, where $\Delta\rho = \rho_2 - \rho_1$. Considering heterogeneity of the cross section of a real channel, the obtained deviation must be multiplied by 0.1 [4]:

$$\xi \sim 10|\Delta\rho| \text{ rad}$$

If we assume that the CES is not sensitive to gravity, deflection of the cupula due to the force of gravity should be less than or equal to that caused by threshold acceleration of the CES [14]: $10|\Delta\rho| \sim 10^{-5}$ rad, hence $|\Delta\rho| \sim 10^{-6}$ g/cm^3. The obtained value for $|\Delta\rho|$ has an order of fluctuating changes in density and, according to [13], it is beyond the margin of error of their experimental determination. When endolymph and the cupula differ in density, this estimate appears to be considerably low. In the case of $|\Delta\rho| > 10^{-6}$ g/cm^3, it should be considered that the CES is sensitive to gravity, and this enables us to assume that the difference in densities of the cupula and endolymph elicits the Ledoux effect [10]. Threshold sensitivity of the horizontal canal is considerably higher than that of the vertical one. In this case, during rotations with inclination, in which the canals change places functionally, the effect of density difference (EDD) should increase. However, even with such a low $\Delta\rho$, EDD may be manifested under certain conditions, for example during spaceflights. Indeed, let us use the solution to equation (14) for the case where the axis of rotation is perpendicular to the plane of the torus and is situated at distance λ from its center (case B.1). Assuming that $t \to \infty$ and $\varphi_{\gamma_i} = 0$ in (15), we shall have:

$$|\zeta| = \left| \frac{\alpha\omega^2}{\omega_0^2} \right|. \qquad (18)$$

Since $\lambda \sim 10^9$ cm and $\omega \sim 10^{-3}$ s^{-1} under these conditions, $|\xi| \sim 10^{-5}$ rad.

The obtained deviation is of the same order as displacement of the cupula at threshold accelerations under ordinary conditions. Thus, it is possible that EDD is one of the factors that cause impairment of CES function during spaceflights. According to (18), it also follows that within the limits of the proposed model, deviation of the cupula upon rotation of the CES may be either positive or negative. This means that the cupula can shift in both the direction of rotation and counter to it. The direction of the shift depends on the signs of $\Delta\rho$, λ, and sign of φ_η.

Using the obtained estimate of $\Delta\rho$, let us determine the correlation between angular velocity and distance between axis of rotation and center of canal at which EDD will be manifested. We shall limit ourselves to consideration of rotation at a constant angular velocity, since in this case equation of movement (6) can be analytically solved with accuracy in a linear approximation. The condition for manifestation of EDD is when displacement of the cupula exceeds its threshold deviation: $|\xi| > 10^{-5}$ rad. From equation (18) we have $\lambda\omega^2 > 10^3$ cm/s^2.

Thus, in order to observe the EDD with the normal range of angular velocities used in cupulographic studies (up to 1 s^{-1}), the distance from the axis of rotation to the center of the semicircular canal must be greater than 10^3 cm.

Let us discuss some of the manifestations of EDD when $\Delta\rho$ has the margin of error of experimental determination of densities of the cupula and endolymph: $|\Delta\rho| \sim 10^{-4}$ g/cm^3. In addition to the above-mentioned manifestations of EDD with periodic rocking of the CES (cases A.2 and B.2), additional effects arise. According to the solutions to equations (9) and (16), frequencies that are multiples of the exogenous perturbation arise in cupular oscillation. In case B.2 ($\varphi_\eta = 0$), considering that $A/\nu \simeq 1$ rad, $\nu \simeq \omega_0/2$, according to (17) considering heterogeneity of canal cross section, we shall have: $\varepsilon L \sim 10^{-7}\lambda$, $\varepsilon L_2 \sim 10^{-9}\lambda$. Consequently, with $|\Delta\rho| \sim 10^{-4}$ g/cm^3, the CES will demonstrate oscillations with a dual frequency at distance $\lambda \geqslant 10^2$ cm between the axis of rotation and center of the torus. In case A.3, with the used amplitude and frequency of exogenous perturbation, according to (13) cupular oscillations arise in relation to the shifted position of equilibrium at an amplitude of $\sigma a \leqslant 10^{-5}$ rad and frequency ν.

This example indicates that, due to EDD, the vertical and horizontal canals may yield contradictory information about the true parameters of the exogenous factor.

Thus, when the densities of the cupula and endolymph differ, the CES becomes sensitive to linear accelerations, change in position of the cupula during

constant rotation, and multiple frequencies appear in cupular oscillations. In the case of experimental confirmation of EDD, the above distinctions in CES dynamics may alter appreciably conceptions concerning the function of the system of semicircular canals and be one of the possible causes of vestibular disturbances during exposure to periodic exogenous factors and altered gravity.

It should be noted that the range of manifestation of effects of the EDD type may be appreciably wider than the one we have discussed: from processes related to inertial separation of ions differing in mass in endolymph to changes in cupular dynamics with caloric stimulation of the vestibular system due to differences in coefficients of thermal dilatation of the cupula and endolymph. The latter circumstance may be the cause of caloric nystagmus in weightlessness.

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METHOD OF MEASURING PHOSPHOLIPASE ACTIVITY IN DUODENAL CONTENTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by I. L. Medkova, N. M. Nikolayeva, K. V. Smirnov and B. P. Surinov]

[Text] It is known that spaceflight factors affect the function of digestive organs [7]. There are data concerning change in activity of pancreatic lipase (triacylglycerol lipase, EC 3.1.1.3) and monoglyceride lipase (monoacylglycerol lipase, EC 3.1.1.23) in animals after both hypokinesia and real spaceflights [4, 6]. Of the set of lipolytic enzymes, an important role is played by pancreatic phospholipase A-2 (phosphatide-2-acylhydrolase, EC 3.1.1.4), which splits unsaturated fatty acid in the 2 position from the lecithin molecule. There have been virtually no studies of its activity following exposure to extreme factors. One of the reasons for this is the methodological difficulty of analyzing phospholipase A-2.

We know of methods of measuring phospholipase activity in agar plates with egg lecithin (semiquantitative method) by means of titration or potentiometry of fatty acids released upon enzymatic hydrolysis of lecithin, etc. [1, 9]. All of these methods have some flaws or other, which include, in particular, poor accuracy and low sensitivity, need to use a special substrate (chemical modifications of lecithin), and they are time consuming. For this reason, it is deemed necessary to work out a specific, colorimetric and easy method of analyzing phospholipase A-2.

We propose here a spectrophotometric method of measuring enzymatic activity of phospholipase A-2 in duodenal contents.

One of the important stages in working out a method of measuring phospholipase A-2 activity was the choice of substrate. Efforts to use purified lecithin produced by Serva (FRG) did not yield satisfactory results: hydrolysis was inefficient and there was a low yield of free fatty acid. We were able to obtain the required substrate mixture only by using egg lecithin in natural compositions after emulsification of egg yolk in the presence of Ca^{2+} ions and deoxycholate. Its formula is essentially similar to the ones used by other authors [10].

It is known that enzymatic catalysis occurs the fastest when there is an optimum proportion of enzyme and substrate. We tested different dilutions

of emulsified egg yolk. We found that 20-fold dilution is the optimum in the variant of the method tested for duodenal contents. To rule out the possibility of lecithin hydrolysis by other phospholipases, the latter are denatured by preheating of samples at 75°C. Phospholipase A-2 remains active [8]. Heat treatment of the sample and naturally occcurring lecithin compositions emulsified in the substrate mixture provide for the specificity of this technique for measuring activity of phospholipase A-2.

Phospholipase A-2 is synthesized in the pancreas in the form of zymogen [1], which is activated by proteases upon entering the duodenum. In order to measure the full activity of phospholipase A-2 it is necessary to activate the enzyme, to convert all of the zymogen to an active form. One uses activation by autologous proteases [1], or else pure trypsin is added to the specimen [8]. A comparison of these two methods of activating phospholipase A-2 revealed that long-term incubation is required for activation by autologus enzymes. This is associated with partial decline of phospholipase activity, perhaps due to digestion of enzyme molecules. For this reason, we chose the method of conversion of zymogen into active enzyme by adding trypsin to the specimen.

The next stage of the method is incubation (at 37°C) of the mixture of substrate and specimen, during which there is enzymatic splitting of fatty acid from lecithin in position 2. Activity of the enzyme is assessed from the quantity of free fatt acids in the enzyme-substrate mixture. Along with enzymatic splitting, there is also spontaneous separation of fatty acids from lecithin, which is manifested by accumulation of free fatty acids in the blank sample. For this reason, incubation time should be sufficient for manifestation of enzymatic activity with minimal increment of free fatty acid in the blank sample. Optimum results are obtained with 1.5-h incubation. With a substrate prepared from egg yolk, the amount of liberated fatty acids is determined by titration or potentiometry [1, 9]. We used for this purpose a method of measuring them in the form of copper salts stained with chromogenic complexing agent and extracted with organic solvent. Sodium diethyldithiocarbamate, which had been previously used for analysis of pancreatic lipase [3] and monoglyceride lipase [5], was used as chromogenic complexing agent. Thus, the exact amount of fatty acids released under the effect of the enzyme can be measured with a spectrophotometer or photoelectric colorimeter. The advantage of such analysis is that the same procedures are used for analysis of three different lipolytic enzymes--pancreatic lipase, monoglyceride lipase and phospholipase. Productivity, sensitivity and precision of the test are improved.

The proposed method of measuring activity of phospholipase A-2 can be used to investigate the effect of extreme factors on function of the system of digestive organs, including tests in clinical laboratories, since we know [2] that its activity changes appreciably in the presence of a number of pathological states (acute pancreatitis, heart and kidney diseases).

Methods

Equipment: Spectrophotometer (SF-26 and others) or photoelectric colorimeter (FEK-56 and others); incubator (37°C); magnetic mixer; test tubes with ground-glass stoppers, dishes, racks, etc.

Reagents

1. Deoxycholate solution--20 mg deoxycholic acid in 2.5 mℓ 0.02 n NaOH and 7.5 mℓ water, or 21 mg sodium deoxycholate in 10 mℓ water. Stored at 4°C.

2. Substrate. Hen egg (preferably day-old) yolk (20-23 g), shaken with 100 mℓ 0.9% NaCl solution. The obtained mass is mixed on a magnetic mixer for 10 min, then we add 6 mℓ 3% $CaCl_2$ solution and mixing is continued for another 50 min. The material is filtered through cotton and stored at 4°C (the mixture is stable for 3-4 days). Before use, we add 2.5 mℓ deoxycholate solution to 10 mℓ of this mixture, then dilute it in water 20-fold and add 187.5 mℓ water.

3. Tris-buffer, pH 8.0. In a graduated 500-mℓ flask, 3.45 g tris-buffer was dissolved in 15 mℓ 1 n, HCl, pH 8.0 was established, and volume brought up to the mark with water.

4. Extraction solution--mixture of chloroform and heptane in a 3:2 ratio. Stored in a dark place.

5. Saturated sodium bromide solution; 51 g NaBr and 50 mℓ water mixed for 1 h on the magnetic mixer, allowed to stand overnight and filtered.

6. Copper reagent. In a 100-mℓ graduated flask, 5 mℓ 1 M acetic acid is mixed with 7.6 mℓ triethanolamine and 2.38 g C_i [?] $(NO_3)_2 \cdot 3H_2O$, dissolved in 60 mℓ water and 25 g NaCl added. The volume is brought almost to the mark with water, pH 8.3 is established with 1 M acetic acid or triethanolamine and finally water is added to bring volume up to the mark.

7. Staining reagent. In a 100-mℓ graduated flask, 100 mg sodium diethyldithiocarbamate is dissolved in 60 mℓ n-butanol and chloroform is used to bring volume up to the mark. The obtained reagent is stored at 4°C in a beaker with ground-glass stopper, in the dark, for 4-5 days.

8. Standard oleic acid solution (6 μmol/ℓ). In a 100-mℓ graduated flask, 170 mg oleic acid is dissolved in extraction solution and volume brought up to the mark (mother liquor). The obtained solution is stored at 4°C in a beaker with ground-glass stopper. Before use, the mother liquor is diluted 100-fold in extraction solution (60 μmol/ℓ).

Preparation of specimen

To 1 mℓ sample (portion A of duodenal contents) we add 0.5 mℓ 0.1 M$CaCl_2$ (0.55 g $CaCl_2$ in 100 mℓ water), heat the mixture for 10 min in a water bath at 75°C, then cool it to room temperature and add 0.5 mℓ trypsin solution (60 mg in 1 ℓ tris-buffer). The obtained sample is incubated for 30 min at 37°C and quickly cooled (placed in freezer for 10 min).

Analysis

Experimental sample: to 1 mℓ substrate in a test tube with ground-glass stopper we add 0.1 mℓ duodenal juice and incubate the mixture for 1.5 h at 37°C. The

reaction is stopped by addition of 7 mℓ extraction solution, the mixture is vigorously agitated for 3 - 4 min. We add 1 mℓ saturated sodium bromide solution and 3.5 mℓ copper reagent to the test tube. The test tube is shaken for 0.5 min (prolonged shaking could lead to emulsification), allowed to stand, a 3-mℓ sample is taken from the top phase filtered through a paper filter and to it we add 0.5 mℓ stain. The samples are immediately submitted to photometry at 435 nm (during work direct sunrays should be prevented from reaching the material).

Determination is also made of extinction of the blank sample. The extraction solution, which is kept in a test tube with ground-glass stopper, is added to the substrate before the tested sample (duodenal juice), then all of the reagents are added in the same order as to the experimental sample. Extinction of the experimental and vacant samples is determined in comparison to a control mixture containing all reagents, with the exception of substrate and duodenal juice. Extinction of the standard is determined in the same way. Instead of the substrate-enzyme mixture, 7 mℓ standard (60 μmol/ℓ) oleic acid solution is placed in a test tube with ground-glass stopper, then all of the reagents are added in the same order as in the experimental sample and blank.

Calculation of Activity

Phospholipase A-2 activity is expressed in micromoles fatty acid released from the substrate under the effect of the enzyme present in 1000 mℓ duodenal contents, for 1 min at 37°C.

Analysis of phospholipase A-2 activity in different dilutions of duodenal contents revealed that, within the range of 0 to 1.0, extinction is a linear function of dilution (enzyme content in the sample). The calibration curve, i.e., extinction as a function of concentration of oleic acid in the sample, has the same shape. For this reason, calculation of activity of phospholipase A-2 in duodenal contents can be made using the following formula:

$$E = \frac{A_1 - A_2}{A_3} \cdot 0.42 \cdot \frac{V_0}{V_1} \cdot \frac{1}{T} \cdot X$$

where E is activity of the tested sample (in μmol/min·ℓ); A_1, A_2 and A_3 is extinction of experimental, blank samples and standard, respectively; 0.42 is quantity of oleic acid in the standard (in μmol); V_0 is 1000 mℓ duodenal contents; V_1 is volume of tested sample; T is sample incubation time (in min); P [sic] is dilution of tested sample.

After simplification, the formula acquires the following appearance:

$$E = \frac{A_1 - A_2}{A_3} \cdot 93.33$$

In a study of normal range in 18 essentially healthy individuals 25 to 40 years of age, phospholipase A-2 activity in portion A of duodenal contents ranged from 20 to 80 μmol/min/ℓ and constituted a mean of 50.8±3.6 mol/min/ℓ. The method has a 2% margin of error and sensitivity to 1 μmol fatty acid; the time required for analysis of 15 samples is 4 h.

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POLAROGRAPHIC METHOD OF MEASURING LIPID PEROXIDATION PRODUCTS IN PLASMA AND ERYTHROCYTES OF MAN AND LABORATORY RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by A. Ye. Zezerov and S. M. Ivanova]

[Text] The process of lipid peroxidation (LPO) plays a part in physiological pathological reactions [1, 2, 8-11].

Use of different methods of demonstrating LPO products does not always yield unambiguous results when studying the effect of the same factor [1]. In the opinion of some authors [5, 7], the most adequate methods of evaluating LPO levels in vivo are methods for measuring the concentrations of primary molecular products (hydroperoxides and diene conjugates), as well as end LPO products of the fluorescent Schiff base type [3, 14, 15].

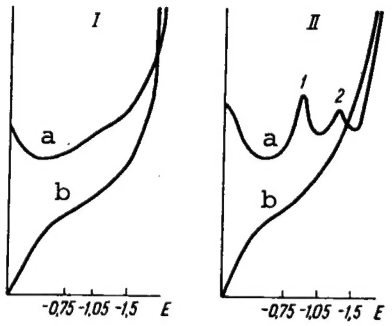
We describe here a study of levels of primary molecular and end products of LPO using polarography with mercury-drop electrode [3, 4] in human and animal plasma and erythrocytes.

Methods

The studies were pursued on 9 subjects 30-35 years of age. Plasma and red cells were taken from venous blood drawn on a fasting stomach. In the animal experiment, we used white male Wistar rats (12 animals) weighing 200 g, which were sacrificed by decapitation. Plasma and erythrocyte suspension were fixed in 0.02% alcohol solution of the synthetic antioxidant, ionol (2,6-di-tert-butyl-4-methylphenol) to prevent further oxidation of lipids, then frozen in dry ice and stored at a temperature of -40°C. Lipids were extracted from plasma by the Keyts method [6]. The extracting mixture of methanol and chloroform (2:1) contained 0.001% ionol. Lipids were isolated from red blood cells by the same method in our modification, which involved separate addition of methanol and chloroform for more complete extraction of lipids. All operations were performed under refrigeration. Lipid concentration was measured by gravimetry.

Polarographic analysis was performed in a system of solvents, methanol and benzene (2:1), and 0.25 M LiCl using a P-8 Janagimoto (Japan) polarograph. Concentration of lipid hydroperoxides was calculated from the diffuse current

at a potential of halfwave $E_{0.5}$ in the range of -0.75:-1.05 V and end products of LPO at $E_{0.5}$ in the range of -1.05:-1.5 V. The measurement results were expressed in the following units: for lipid hydroperoxides, in nanomoles per mg lipids; for end products of LPO in nanoamperes per mg lipids. Capillary constant $m^2/^3t^1/^6$ = 0.86, drip time 1.92 s, m = 0.68 mg/s, constant of diffusion current was taken at 4.182. A typical polarogram is illustrated in the Figure.



Typical polarograms of plasma and erythrocyte lipids; x-axis, half-wave potential (V); y-axis, concentration of peroxides

I) blank sample
II) experimental sample
a,b) differential and integral tracing, respectively
1,2) peak lipid hydroperoxides and end LPO products, respectively

Results and Discussion

The findings are listed in the Table. Analysis of levels of products of free-radical oxidation of lipids revealed a certain level of lipid peroxidation in plasma and erythrocytes. It was found that the LPO levels were higher in human and animal erythrocytes than plasma. Analogous findings were made when we measured hydroperoxides by the method of iodometric titration in experiments on dogs [13].

Examination of the LPO system in different organs and tissues using electronic paramagnetic resonance, polarography and iodometric titration with amperometric recording of equivalence point established that there were different concentrations of free radicals and endogenous products of free-radical oxidation of lipids in different organs and tissues, and it was shown that actively metabolizing tissues were characterized by higher levels of LPO processes [7, 8, 12].

LPO levels in human and animal plasma and erythrocytes

Tested parameter	Subjects		Rats	
	plasma	red cells	plasma	red cells
Lipid hydroperoxides, nM/mg lipids	3,11±0,25 (n = 9)	5,93±0,37 (n = 8)	2,32±0,1 (n = 12)	6,29±0,54 (n = 9)
End LPO products, nA/mg lipids	28,26±3,32 (n = 9)	48,66±4,56 (n = 8)	39,32±2,76 (n = 11)	74,67±7,07 (n = 9)

The high LPO level in red blood cells, as compared to plasma, is apparently related to lower concentration in these cells of α-tocopherol [16], natural

antioxidant and insignificant damage to the erythrocyte membrane due to freezing and thawing.

The proposed method permits measurement of hydroperoxides of all lipids and end products of LPO, and it can be used to study the distinctions in reactions of free-radical oxidation in the body when exposed to extreme factors.

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MEANS OF DEVELOPING INTENSIVE STRAIN OF WHEAT FOR HUMAN LIFE-SUPPORT SYSTEM

[Synopsis of Article by V. I. Polonskiy and G. M. Lisovskiy]

[Text] A solution to such an important problem as reducing the size of space greenhouses can be found by using plants exposed to intensive radiation at levels of photosynthetically active radiation (PAR) exceeding the maximum solar radiation on earth, as well as highly productive cultivars specially adapted to such conditions.

Individual selection from wheat variety 232 was made for grain content of spike against a background of high PAR levels in order to find light-resistant highly productive forms of plants, and they were tested for resistance of the photosynthetic system to high levels of irradiation. Wheat was grown by the hydroponic method on claydite in a vegetation box that could be sealed at PAR of 1300 W/m^2.

Under the effect of high levels of PAR, a few plants appeared in the wheat population that differed drastically in grain content of spikes, which exceeded the mean by 1.6-2.0 times. Line No 5 was obtained as a result of individual selection from such a "base" plant in four generations. A comparison of this wheat line in the fifth and sixth generations to the original variety 232 was made at PAR levels of 800-1300 and 500-600 W/m^2, respectively. Physiological assessment of the plants led us to conclude that the parameters of water conditions were better in line No 5 than in the original cultivar 232: 11% more water in the upper leaves, 13% less water shortage, 1/4th the diffusion resistance of leaves. Chlorophyll and carotenoid content, as well as the share of poorly bound chlorophyll a, were substantially higher in leaves of line No 5 than in the initial cultivar. The greater resistance in line No 5 plants of the photosynthetic system to high intensity PAR enabled them to form a larger general biomass and yield a larger crop of grain. A grain yield of

5 kg/m^2 was obtained from line No 5 in 65 days of vegetation, versus 3.5 kg/m^2 for the initial cultivar, with plant density of 4000 plants/m^2 and PAR intensity of 800-1300 W/m^2. For the yield recovered from line No 5 with high-intensity PAR, in order to fully furnish man with oxygen, water, as well as bread (400 g/day), as much photosynthetically active radiation will be required as comes from the sun on only 6 m^2 of a normally oriented area. This study, even on the example of one variety of wheat and limited number of selection characters, graphically shows that plant breeding is one of the realistic means of intensifying the photosynthetic process in the phototrophic element of a life-support system. 2 tables, 12 references.

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